



NEWSLETTER



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Addict Behav. 2013 Sep;38:2415-21.

PROSPECTIVE EFFECTS OF ADOLESCENT INDICATORS OF BEHAVIORAL DISINHIBITION ON DSM-IV ALCOHOL, TOBACCO, AND ILLICIT DRUG DEPENDENCE IN YOUNG ADULTHOOD.

Palmer RH, Knopik VS, Rhee SH, et al.

OBJECTIVE: To identify robust predictors of drug dependence.

METHODS: This longitudinal study included 2361 male and female twins from an ongoing longitudinal study at the Center for Antisocial Drug Dependence (CADD) at the University of Colorado Boulder and Denver campuses. Twins were recruited for the CADD project while they were between the ages of 12 and 18. Participants in the current study were on average approximately 15years of age during the first wave of assessment and approximately 20years of age at the second wave of assessment. The average time between assessments was five years. A structured interview was administered at each assessment to determine patterns of substance use and Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; Fourth Edition) attention deficit hyperactivity disorder (ADHD), conduct disorder (CD), and drug dependence symptoms. Cloninger's Tridimensional Personality Questionnaire was also used to assess novelty seeking tendencies (NS). At the second wave of assessment, DSM-IV dependence symptoms were reassessed using the same interview. Path analyses were used to examine direct and indirect mechanisms linking psychopathology and drug outcomes.

RESULTS: Adolescent substance use, CD, and NS predicted young adult substance dependence, whereas the predictive effects of ADHD were few and inconsistent. Furthermore, CD and NS effects were partially mediated by adolescent substance use.

CONCLUSIONS: Adolescent conduct problems, novelty seeking, and drug use are important indices of future drug problems. The strongest predictor was novelty seeking.

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Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase, PsycINFO e PsycArticle utilizzando le seguenti parole chiave (o i loro sinonimi): 'Attention deficit disorder', 'Attention deficit hyperactivity disorder', 'Infant', 'Child', 'Adolescent', 'Human'. Sono qui riportate le referenze considerate rilevanti e pertinenti.

Addictive Behaviors. 2013.

ADHD, STIMULANT TREATMENT IN CHILDHOOD AND SUBSEQUENT SUBSTANCE ABUSE IN ADULTHOOD - A NATURALISTIC LONG-TERM FOLLOW-UP STUDY.

Dalsgaard S, Mortensen PB, Frydenberg M, et al.

The purpose of the study was to estimate the risk of substance use disorder (SUD) and alcohol abuse in adulthood among children and adolescents with attention-deficit hyperactivity disorder (ADHD) compared to the background population. Furthermore, to examine whether the age at initiation and duration of stimulant treatment in childhood predicts SUD and alcohol abuse in adulthood. 208 youths with ADHD (183 boys; 25 girls) were followed prospectively. Diagnoses of SUD and alcohol abuse were obtained from The Danish Psychiatric Central Register. The relative risk (RR) of SUD and alcohol abuse for cases with ADHD, compared to the background population was 7.7 (4.3-13.9) and 5.2 (2.9-9.4), respectively. Female gender, conduct disorder in childhood and older age at initiation of stimulant treatment increased the risk of later SUD and alcohol abuse. Our results warrant increased focus on the possibly increased risk of substance abuse in females with ADHD compared to males with ADHD.

Am J Med Genet Part B Neuropsychiatr Genet. 2013;162:718-33.

ASSOCIATION OF GENETIC RISK SEVERITY WITH ADHD CLINICAL CHARACTERISTICS.

Kotte A, Faraone SV, Biederman J.

This study sought to examine the association between the cumulative risk severity conferred by the total number of attention-deficit/hyperactivity disorder (ADHD) risk alleles of the DAT1 3'UTR variable number tandem repeat (VNTR), DRD4 Exon 3 VNTR, and 5-HTTLPR with ADHD characteristics, clinical correlates, and functional outcomes in a pediatric sample. Participants were derived from case-control family studies of boys and girls diagnosed with ADHD, a genetic linkage study of families with children with ADHD, and a family genetic study of pediatric bipolar disorder. Caucasian children 18 and younger with and without ADHD and with available genetic data were included in this analysis (N=591). The association of genetic risk severity with sociodemographic, clinical characteristics, neuropsychological, emotional, and behavioral correlates was examined in the entire sample, in the sample with ADHD, and in the sample without ADHD, respectively. Greater genetic risk severity was significantly associated with the presence of disruptive behavior disorders in the entire sample and oppositional defiant disorder in participants with ADHD. Greater genetic risk severity was also associated with the absence of anxiety disorders, specifically with the absence of agoraphobia in the context of ADHD. Additionally, one ADHD symptom was significantly associated with greater genetic risk severity. Genetic risk severity is significantly associated with ADHD clinical characteristics and co-morbid disorders, and the nature of these associations may vary on the type (externalizing vs. internalizing) of the disorder.

Am J Psychiatry. 2013;170:1205-11.

ASSOCIATION BETWEEN VARIATION IN NEUROPSYCHOLOGICAL DEVELOPMENT AND TRAJECTORY OF ADHD SEVERITY IN EARLY CHILDHOOD.

Rajendran K, Trampush JW, Rindskopf D, et al.

Objective: This longitudinal study examined if changes in neuropsychological functioning were associated with the trajectory of symptoms related to attention deficit hyperactivity disorder (ADHD) and impairment between preschool and school age.

Method: The sample consisted of 3- and 4-year-old children (N=138) who were identified as being at risk for ADHD based on parent and teacher reports. Neuropsychological functioning was measured annually using the NEPSY at four time points (mean ages, 4.19, 5.36, 6.35, and 7.35 years). ADHD symptoms and impairment were assessed with semiannual parent and teacher reports using the ADHD Rating Scale-IV and the Children's Problems Checklist at 10 time points (mean ages at baseline and final assessment, 4.19 and 8.81 years, respectively). Hierarchical linear modeling was used to assess the trajectories of change in

neuropsychological functioning and ADHD severity as well as the association of change in neuropsychological functioning with change in ADHD severity over time.

Results: Baseline neuropsychological functioning was not significantly associated with the slope of change in ADHD severity. However, the magnitude of change in neuropsychological functioning was linearly associated with the trajectory of ADHD symptom severity and impairment, such that individuals with greater neuropsychological growth over time had a greater diminution of ADHD severity and impairment. Family socioeconomic status at baseline was significantly associated with initial ADHD severity and impairment, but not with change over time.

Conclusions: Interventions that enhance neuropsychological functioning at an early age may be beneficial in attenuating longterm ADHD severity and impairment.

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Behav Ther. 2013.

PARENTING BEHAVIORS DURING RISKY DRIVING BY TEENS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Schatz NK, Fabiano GA, Morris KL, et al.

Parenting practices for teen drivers with ADHD were observed via a video monitor installed in vehicles. All teens had recently completed a driver education course and were in the driving permit stage of a graduated driver-licensing program. Parent behaviors were coded during drives when teens were driving safely and during drives when teens engaged in risky driving. The overall frequency of positive parenting strategies was low, regardless of whether teens drove safely or engaged in risky driving. Although the rate of negative feedback was also low, parents engaged in significantly more criticism and were rated by an observer to appear angrier when teens were driving in a risky manner. No other differences in parent behaviors associated with the quality of teen driving were observed. The inconsistencies between observed parenting behaviors and those parenting practices recommended as effective with teens with ADHD are discussed. The need for further research addressing effective strategies for teaching teens with ADHD to drive is highlighted.

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Behav Neurol. 2013;27:341-42.

NEUROFEEDBACK TRAINING FOR CHILDREN WITH ADHD: RECENT ADVANCES AND NEW APPLICATIONS.

Drechsler R.

Neurofeedback training (NF) has found increasing acceptance as a non-pharmacological treatment for children with Attention Deficit Hyperactivity Disorder (ADHD). NF aims at the regulation of electrical brain activity patterns. In the first talk, a summary of the most influential multicentre training study of the recent years will be given, including long-term outcome data and results from new follow-up studies with the application of NF to Tic Disorder (H. Heinrich). nullClassicnull protocols of NF frequency training, which are aimed at the improvement of attentional control, feed back activity of theta or beta bands. The feed back of gamma-band activity is a new approach (T. Bogen). Though technically challenging, gamma-band NF promises to be an efficacious treatment for emotion regulation deficits, a frequent comorbidity of children with ADHD. The third presentation introduces tomographic neurofeedback training for children with ADHD (D. Brandeis). In tomographic NF, the activation of a determined brain region is calculated and fed back to the individual, in contrast to conventional NF, which uses electrical activity at the scalp surface. Finally, the importance of choosing an appropriate control condition for the analysis of NF treatment specificity will be discussed in the last talk (R. Drechsler). A differential EMG (electromyogram) biofeedback training is proposed as control condition that seems preferable from an ethical point of view to sham NF control.

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Behav Neurol. 2013;27:344.

EFFICACY OF NEUROFEEDBACK TRAINING IN ADHD: THE IMPORTANCE OF APPROPRIATE CONTROL CONDITIONS.

Drechsler R, Brandeis D.

GOALS: Although the beneficial effects of neurofeedback (NF) training on ADHD symptoms are beyond doubt, the mechanisms leading to these effects remain unclear. Control conditions are critical to determine specific effects of NF in randomized controlled trials. The majority of controlled studies have included semi-active or active control conditions where NF is compared to treatments such as medication, computerbased cognitive programs or behavioural therapy. Only a minority of studies have used nullshamnull NF as control condition. The methodological and ethical problems of these studies, which failed to demonstrate the superiority of nullshamnull compared to nullshamnull NF, will be discussed. Other biofeedback methods, such as electromyogram biofeedback (EMG-BF) are presented as alternatives.

METHODS: A differential EMG-BF protocol which feeds back activity from arm muscles involved in fine motor skills such as writing and grip was developed as a control condition for a complex tomographic neurofeedback protocol. Two groups of children with ADHD were trained with EMG-BF or NF over the same period of time, using the same training software and matching protocols.

RESULTS: A clinically relevant reduction of ADHD symptoms was observed in both groups of children. Specific effects were found for the EMG-BF group in neuropsychological tests related to fine motor skills and bimanual coordination. Only trends were found for specific electrophysiological treatments effects in the NF group.

DISCUSSION: EMG-BF represents a valuable control condition with a meaningful motor coordination and skill training for children with ADHD. Ethical as well as methodological aspects have to be considered when conducting clinical trials conform to standards of evidence-based medicine.

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Behav Neurol. 2013;27:448-49.

FETAL ALCOHOL SPECTRUM DISORDERS (FASD) CHILDREN WITH ADHD HAVE IMPAIRED WORKING MEMORY AND BEHAVIORAL PROBLEMS COMPARED TO IDIOPATHIC ADHD.

Corredera A, Campabadal A, Boix C, et al.

OBJECTIVE: Prenatal alcohol exposure can cause alterations to neurodevelopmental brain. Several studies have described difficulties in many cognitive functions and more specifically in IQ, attention and executive functions. Individuals with prenatal alcohol exposure are at increased risk for ADHD. According to the ADHD ethology, children show different cognitive and behavioral profiles. As reported, children with ADHD related to prenatal alcohol consumption show greater severity and incidence of social adjustment difficulties in comparison to idiopathic ADHD. The present study aims to assess working memory as well as behavioral problems in children with FASD/ADHD in comparison with idiopathic ADHD.

METHODS: 17 adopted children diagnosed of FASD/ ADHD, age ranged between 6 and 10 years, were compared with 17 idiopathic ADHD children. Both groups were matched by the same subtype of ADHD, age and sex. Working memory was assessed using Digits, Letter and Number and Arithmetic subtests of the WISC-IV. Behavior problems were assessed using the Achenbach's Child Behavior Checklist for Parents and Teachers (CBCL).

RESULTS: Statistical analysis using T student shows significant differences between both groups in Digits ($p < 0.004$), Letter and number ($p < 0.003$) and Arithmetic ($p < 0.000$) WISC-IV subtest. In related to behavioral problems, we found only significant differences in social problems subscale in teacher's CBCL ($p < 0,037$).

CONCLUSION: FASD/ADHD children tend to have more cognitive and behavioral problems compared to probable idiopathic ADHD. This profile is the one described in the Fetal Alcohol Spectrum Disorders. These differences in neuropsychological profile can contribute to improve the differential diagnosis, the intervention and outcome between both groups. We recommend a routine monitoring FASD/ADHD to implement therapeutic interventions as early as possible.

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Behav Neurol. 2013;27:342.

STANDARD NEUROFEEDBACK PROTOCOLS IN CHILDREN WITH ADHD: METHODOLOGICAL INTRODUCTION AND RESULTS FROM CLINICAL STUDIES.

Heinrich H.

GOALS: Neurofeedback (NF) may be interpreted as a neuro-behavioural treatment for attention-deficit/hyperactivity disorder (ADHD) where children learn to modulate specific brain electrical activity patterns and how to apply their neuroregulation strategies in daily life. Training of slow cortical potentials (SCPs) and theta (4-7 Hz)/beta (13-20 Hz) training are considered as standard protocols.

METHODS: At the conference, the methodical basis of these protocols integrated into a hypothetical model of 'active ingredients' will be presented. NF studies of our group will be reflected with a focus on the up-to-now largest randomised controlled trial (about 100 children included) comparing NF (combination of SCP and theta/beta training) with a computerised attention training.

RESULTS: In this trial, NF was superior to the control training in reducing severity of ADHD symptoms at post-training as well as at 6-month follow-up (medium effect size). Parents of both groups did not differ on evaluation scales which were applied to control for attributional effects. At the neurophysiological level, differential patterns for SCP and theta/beta training were obtained. In a second study on SCP training, a significant relationship between regulation skill and clinical outcome was obtained. In a third study, SCP training was superior to a theta/low-beta (12-15 Hz) training in reducing ADHD behaviour in children with tic disorders. Mainly, hyperactive/impulsive symptoms were observed to be reduced probably due to the fact that transfer into daily life focused on inhibition of behaviour (i.e. tic suppression).

CONCLUSIONS: There is clear evidence for specific effects of NF (SCP and theta/beta training) in ADHD so that NF based on these standard protocols may be supported as a treatment for ADHD. However, medium effect sizes indicate that NF should not be seen as a stand-alone intervention but rather as a module within a multimodal treatment tailored to the needs of a child.

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Behav Neurol. 2013;27:311.

SELF-AWARENESS IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: FURTHER EVIDENCE OF THE POSITIVE ILLUSORY BIAS.

Volz-Sidiropoulou E, Bocker M, Gauggel S.

OBJECTIVE: This study aimed to examine the accuracy of self-reports of children and adolescents with attention-deficit/hyperactivity disorder (ADHD) in evaluating their competence in every-day activities.

METHOD: Self-reports of children and adolescents with ADHD (n=89) were compared with those of non-referred children (n=94), and also to parental reports of their children's competence in performing daily activities. Competence was measured with a 34-item rating scale. Behavioural disorders were documented with the Child Behaviour Checklist.

RESULTS: Children and adolescents with ADHD were much more likely than controls to overestimate their competence in certain daily life activities relative to their parents' reports, demonstrating a positive illusory bias. The positive illusory bias was found to be moderated by coexisting behavioural problems and was pronounced in activities that were expected to be affected by ADHD symptoms. Overestimated self-perceptions of competence were more likely to be accompanied with externalizing problems such as aggression.

CONCLUSION: Results support the presence of the positive illusory bias also in the domain of everyday life activities. In behavioural treatment programs, improvement of self-evaluation of competencies should also become a focus of treatment.

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Behav Neurol. 2013;27:343.

TOMOGRAPHIC NEUROFEEDBACK IN ADHD.

Brandeis D, Drechsler R.

GOALS: Controlled EEG-neurofeedback studies reporting sizeable clinical effects on ADHD (attention deficit/hyperactivity disorder) often fail to distinguish unspecific contributions from specific ones due to learned regulation of neurophysiological measures. Topographic EEG and source localization allows real time estimation and feedback of activity from specific dysfunctional regions. We targeted regulation in the anterior cingulate (ACC), a deep brain region affected in ADHD, as a new approach to increase specificity.

METHODS: In a tomographic neurofeedback (tNF) study, 13 ADHD children trained bidirectional regulation of their ACC brain activity during 36 lessons for theta and beta frequency bands and for slow cortical potentials (SCP). The ACC activity and its change over the course of the training and rest phases were computed using sLORETA (low-resolution electromagnetic tomography) of the 30-channel EEG.

RESULTS: Despite reducing ADHD symptoms and EEG-artefacts control over ACC activity was learned only in one SCP condition providing simple feedback. Instead, the ACC frequency distribution at rest normalized over the course of the training.

CONCLUSIONS: Clinical improvement and artefact/ movement reduction followed ACC-tNF without substantial learning of control, but with stabilisation and normalisation of oscillatory ACC activity at rest. Further studies need to test whether tNF can induce learning in brain regions implicated in ADHD. The assumption that targeting impaired brain regions in clinical groups for self regulation improves learning and outcomes also motivates NIRS- or fMRI-neurofeedback, and still requires critical evaluation.

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Biol Psychol. 2013 Sep;94:12-21.

NEUROFEEDBACK AND STANDARD PHARMACOLOGICAL INTERVENTION IN ADHD: A RANDOMIZED CONTROLLED TRIAL WITH SIX-MONTH FOLLOW-UP.

Meisel V, Servera M, Garcia-Banda G, et al.

The present study is a randomized controlled trial that aims to evaluate the efficacy of Neurofeedback compared to standard pharmacological intervention in the treatment of attention deficit/hyperactivity disorder (ADHD). The final sample consisted of 23 children with ADHD (11 boys and 12 girls, 7-14 years old). Participants carried out 40 theta/beta training sessions or received methylphenidate. Behavioral rating scales were completed by fathers, mothers, and teachers at pre-, post-treatment, two-, and six-month naturalistic follow-up. In both groups, similar significant reductions were reported in ADHD functional impairment by parents; and in primary ADHD symptoms by parents and teachers. However, significant academic performance improvements were only detected in the Neurofeedback group. Our findings provide new evidence for the efficacy of Neurofeedback, and contribute to enlarge the range of non-pharmacological ADHD intervention choices. To our knowledge, this is the first randomized controlled trial with a six-month follow-up that compares Neurofeedback and stimulant medication in ADHD.

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Biol Psychiatry. 2013;74:623-32.

SHARED AND DISTINCT INTRINSIC FUNCTIONAL NETWORK CENTRALITY IN AUTISM AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Di Martino A, Zuo XN, Kelly C, et al.

Background: Individuals with autism spectrum disorders (ASD) often exhibit symptoms of attention-deficit/hyperactivity disorder (ADHD). Across both disorders, observations of distributed functional abnormalities suggest aberrant large-scale brain network connectivity. Yet, common and distinct network correlates of ASD and ADHD remain unidentified. Here, we aimed to examine patterns of dysconnection in school-age children with ASD and ADHD and typically developing children who completed a resting state functional magnetic resonance imaging scan.

Methods: We measured voxelwise network centrality, functional connectivity metrics indexing local (degree centrality [DC]) and global (eigenvector centrality) functional relationships across the entire brain connectome, in resting state functional magnetic resonance imaging data from 56 children with ASD, 45 children with ADHD, and 50 typically developing children. A one-way analysis of covariance, with group as fixed factor (whole-brain corrected), was followed by post hoc pairwise comparisons.

Results: Cortical and subcortical areas exhibited centrality abnormalities, some common to both ADHD and ASD, such as in precuneus. Others were disorder-specific and included ADHD-related increases in DC in right striatum/pallidum, in contrast with ASD-related increases in bilateral temporolimbic areas. Secondary analyses differentiating children with ASD into those with or without ADHD-like comorbidity (ASD+ and ASD-, respectively) revealed that the ASD+ group shared ADHD-specific abnormalities in basal ganglia. By contrast, centrality increases in temporolimbic areas characterized children with ASD regardless of ADHD-like comorbidity. At the cluster level, eigenvector centrality group patterns were similar to DC.

Conclusions: ADHD and ASD are neurodevelopmental disorders with distinct and overlapping clinical presentations. This work provides evidence for both shared and distinct underlying mechanisms at the large-scale network level.

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Biol Psychiatry. 2013;74:599-606.

TRAJECTORIES OF CEREBRAL CORTICAL DEVELOPMENT IN CHILDHOOD AND ADOLESCENCE AND ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Shaw P, Malek M, Watson B, et al.

Background Childhood attention-deficit/hyperactivity disorder (ADHD) persists into adulthood in around half of those affected, constituting a major public health challenge. No known demographic, clinical, or neuropsychological factors robustly explain the clinical course, directing our focus to the brain. Herein, we link the trajectories of cerebral cortical development during childhood and adolescence with the severity of adult ADHD.

Methods Using a longitudinal study design, 92 participants with ADHD had childhood (mean 10.7 years, SD 3.3) and adult clinical assessments (mean 23.8 years, SD 4.3) with repeated neuroanatomic magnetic resonance imaging. Contrast was made against 184 matched typically developing volunteers.

Results Attention-deficit/hyperactivity disorder persisted in 37 (40%) subjects and adult symptom severity was linked to cortical trajectories. Specifically, as the number of adult symptoms increased, particularly inattentive symptoms, so did the rate of cortical thinning in the medial and dorsolateral prefrontal cortex. For each increase of one symptom of adult ADHD, the rate of cortical thinning increased by .0018 mm (SE = .0004, $t = 4.2$, $p < .0001$), representing a 5.6% change over the mean rate of thinning for the entire group. These differing trajectories resulted in a convergence toward typical dimensions among those who remitted and a fixed, nonprogressive deficit in persistent ADHD. Notably, cortical thickening or minimal thinning (greater than $-.007$ mm/year) was found exclusively among individuals who remitted.

Conclusions Adult ADHD status is linked with the developmental trajectories of cortical components of networks supporting attention, cognitive control, and the default mode network. This informs our understanding of the developmental pathways to adult ADHD.

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Biol Psychiatry. 2013;74:585-90.

GEOGRAPHIC VARIATION IN THE PREVALENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: THE SUNNY PERSPECTIVE.

Arns M, Van Der Heijden KB, Arnold LE, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is the most common psychiatric disorder of childhood, with average worldwide prevalence of 5.3%, varying by region.

Methods: We assessed the relationship between the prevalence of ADHD and solar intensity (SI) (kilowatt hours/square meters/day) on the basis of multinational and cross-state studies. Prevalence data for the

U.S. were based on self-report of professional diagnoses; prevalence data for the other countries were based on diagnostic assessment. The SI data were obtained from national institutes.

Results: In three datasets (across 49 U.S. states for 2003 and 2007, and across 9 non-U.S. countries) a relationship between SI and the prevalence of ADHD was found, explaining 34%-57% of the variance in ADHD prevalence, with high SI having an apparent preventative effect. Controlling for low birth weight, infant mortality, average income (socioeconomic status), latitude, and other relevant factors did not change these findings. Furthermore, these findings were specific to ADHD, not found for the prevalence of autism spectrum disorders or major depressive disorder.

Conclusions: In this study we found a lower prevalence of ADHD in areas with high SI for both U.S. and non-U.S. data. This association has not been reported before in the literature. The preventative effect of high SI might be related to an improvement of circadian clock disturbances, which have recently been associated with ADHD. These findings likely apply to a substantial subgroup of ADHD patients and have major implications in our understanding of the etiology and possibly prevention of ADHD by medical professionals, schools, parents, and manufacturers of mobile devices.

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Biol Psychiatry. 2013;74:615-22.

NEUROFUNCTIONAL EFFECTS OF METHYLPHENIDATE AND ATOMOXETINE IN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DURING TIME DISCRIMINATION.

Smith A, Cubillo A, Barrett N, et al.

Background The catecholamine agonists methylphenidate and atomoxetine effectively treat attention-deficit/hyperactivity disorder (ADHD). Furthermore, dopamine agonists have shown to improve time estimation in ADHD, a core cognitive deficit. However, few have compared the effects of methylphenidate and atomoxetine on brain function in ADHD, and none during time estimation. Using single dose challenges, we investigated shared and drug-specific effects in ADHD adolescents on the neural substrates of time discrimination (TD).

Methods Twenty ADHD adolescent male subjects were compared in a randomized double-blind cross-over design after single doses of methylphenidate, atomoxetine, and placebo in functional magnetic resonance imaging during TD. Normalization effects were assessed by comparing brain activation under each drug condition with that of 20 healthy age-matched control subjects.

Results Relative to control subjects, patients under placebo showed TD deficits and reduced activation of ventrolateral prefrontal cortex (VLPFC)/insula, inferior frontal cortex, and supplementary motor area. Performance differences were normalized only by methylphenidate, relative to both atomoxetine and placebo. Both medications, however, significantly upregulated right VLPFC/insula activation within patients and normalized its underactivation in ADHD boys under placebo relative to control subjects. The supplementary motor area and inferior frontal cortex activation differences that were observed under placebo were reduced by methylphenidate and atomoxetine, respectively, but neither survived rigorous testing for normalization.

Conclusions While only methylphenidate had a drug-specific effect of improving TD performance deficits, both drugs significantly upregulated and normalized right VLPFC underactivation in ADHD boys under placebo relative to control subjects, suggesting shared effects of stimulants and nonstimulants on a key prefrontal dysfunction during timing.

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Biol Psychiatry. 2013;74:607-14.

NEURAL MECHANISMS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS ARE STRATIFIED BY MAOA GENOTYPE.

Nymberg C, Jia T, Lubbe S, et al.

Background Attention-deficit/hyperactivity disorder (ADHD) is characterized by deficits in reward sensitivity and response inhibition. The relative contribution of these frontostriatal mechanisms to ADHD symptoms and their genetic determinants is largely unexplored.

Methods Using functional magnetic resonance imaging and genetic analysis of the monoamine oxidase A (MAOA) gene, we investigated how striatal and inferior frontal activation patterns contribute to ADHD symptoms depending on MAOA genotype in a sample of adolescent boys (n=190).

Results We demonstrate an association of ADHD symptoms with distinct blood oxygen level-dependent (BOLD) responses depending on MAOA genotype. In A hemizygotes of the expression single nucleotide polymorphism rs12843268, which express lower levels of MAOA, ADHD symptoms are associated with lower ventral striatal BOLD response during the monetary incentive delay task and lower inferior frontal gyrus BOLD response during the stop signal task. In G hemizygotes, ADHD symptoms are associated with increased inferior frontal gyrus BOLD response during the stop signal task in the presence of increased ventral striatal BOLD response during the monetary incentive delay task.

Conclusions Depending on MAOA genotype, ADHD symptoms in adolescent boys are associated with either reward deficiency or insufficient response inhibition. Apart from its mechanistic interest, our finding may aid in developing pharmacogenetic markers for ADHD.

Br J Dev Psychol. 2013 Sep;31:271-88.

THE ORGANIZATION OF ATTENTION IN TYPICAL DEVELOPMENT: A NEW PRESCHOOL ATTENTION TEST BATTERY.

Breckenridge K, Braddick O, Atkinson J.

This article introduces a new battery of attention tests for typically developing and atypically developing children with a mental age of 3-6 years. In the light of adult and child studies supporting a model of distinct networks for specific attentional operations, tests in the current battery were selected with the aim of measuring functions of selective attention, sustained attention and attentional control (executive function). Normative data were collected from 154 typically developing children aged 3-6 years and examined using exploratory factor analysis to determine latent constructs underlying test performance. This analysis suggested increasing differentiation of attention functions over the age range, with support for the hypothesized three-factor model only after 4(1/2) years of age. Additional analyses supported the validity of the new attention battery with respect to (1) parent/teacher report measures of everyday attention behaviour and (2) later performance on the Test of Everyday Attention for Children (TEA-Ch), a battery designed for children aged 6-16 years. The results show the developing differentiation of attention functions and support the ecological and predictive validity of the battery as providing early performance-based measures of attention and an attention 'profile' for each individual child, which may aid characterization and remediation of neurodevelopmental disorders.

Can J Cardiol. 2013.

EARLY REPAIR OF CONGENITAL HEART DISEASE ASSOCIATED WITH INCREASED RATE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS.

Yamada DC, Porter AA, Conway JL, et al.

Background: As more children survive with congenital heart disease, their neurodevelopmental outcomes (including attention deficit hyperactivity disorder [ADHD]) are becoming increasingly important. The objective of our study was to determine if school-aged children who underwent early cardiac surgery for congenital heart disease are more likely than healthy control subjects to have screening scores on the Swanson, Nolan, and Pelham IV (SNAP-IV) questionnaire suggestive of ADHD.

Methods: Children aged 7-15 years who underwent open-heart surgery before 1 year of age were identified from the Izaak Walton Killam (IWK) Children's Heart Centre Database. Control subjects were recruited from healthy volunteers. The SNAP-IV questionnaire was administered to all participants and a chart review was performed on all eligible children in the cardiac surgery group. Case and control subjects were compared using Fisher's exact test, linear, and logistic regression analyses. Potential predictors of a positive screening score were sought.

Results: A positive screening score was found in 29% (16/56) of the surgical group compared with 3% (2/60) of the control group (P < 0.001). Surgical and control subjects differed in average overall scores

(0.93 vs 0.30; $P < 0.001$) and in scores for hyperactivity (0.83 vs 0.24; $P < 0.001$) and inattention (1.04 vs 0.37; $P < 0.001$). No other significant predictors of a positive screening score were identified. The early open-heart surgery participants who responded to the questionnaire did not differ in baseline characteristics compared with nonresponders.

Conclusions: Children who have open-heart surgery at younger than 1 year of age are more likely than healthy control subjects to have a SNAP-IV score suggestive of ADHD when they reach school age.

Child & Youth Care Forum. 2013 Oct;42:403-24.

THE INCREDIBLE YEARS BASIC PARENT TRAINING FOR PORTUGUESE PRESCHOOLERS WITH AD/HD BEHAVIORS: DOES IT MAKE A DIFFERENCE?

Azevedo AF, Seabra-Santos MJ, Gaspar MF, et al.

Background: Evidence-based psychosocial interventions such as parent training programs are strongly recommended as first-line treatment for preschool-age children with or at-risk of attention deficit/hyperactivity disorder (AD/HD).

Objective: Evaluate the effectiveness of the Incredible Years Basic Parent Training (IY) in hyperactive and inattentive behaviors of Portuguese preschoolers.

Methods: One hundred children, between three and six years-old, with AD/HD behaviors, who were part of a larger randomized controlled trial in which participants were allocated to either an intervention or control group. In this subsample analysis, there were 52 participants in the intervention condition (IYC) and 48 in the waiting-list control condition (WLC). Multi-informants and multi-measures of child and parenting behaviors were taken before and after the 14-week intervention.

Results: Medium-to-large intervention effects were found in primary caregivers' reported measures of children's AD/HD behaviors and on self-reported parenting practices. Independent observations indicated significant short-term effects on positive parenting and coaching. Primary caregivers had a high attendance rate and reported high satisfaction with the program. Additionally, 43 % of children in the IYC clinically improved in the primary AD/HD outcome measure, compared with 11 % in the WLC.

Conclusions: Preliminary results suggest that IY parent training seems to be an effective tool, making the difference in the behavior of Portuguese preschoolers with early signs of AD/HD and their mothers.

Child Adolesc Ment Health. 2013.

WHY ARE CHILDREN AND ADOLESCENTS REFERRED FOR PSYCHIATRIC ASSESSMENT WITHOUT FULFILING DIAGNOSTIC CRITERIA FOR ANY PSYCHIATRIC DISORDER?

Dallos G, Keresztesy A, Miklosi M, et al.

Background: Clinicians often experience that children are referred for psychiatric evaluation without fulfilling the diagnostic criteria of any psychiatric disorders. This study investigates factors that might lead children to psychiatric referral without any psychiatric disorder.

Method: Children/adolescents who were referred for psychiatric assessment (referred group) ($n=418$, mean age = 10.82 years, $SD=3.81$) and a control group ($n=48$, mean age=10.38 years, $SD=3.77$) were evaluated by the Mini International Neuropsychiatric Interview Kid (MINI Kid) and the Erfassung der Lebensqualität Kindern und Jugendlichen (Measure of Quality of Life for Children and Adolescents). The referred group was further divided into two subgroups: referred subgroup without MINI Kid diagnosis ($n=61$) and referred subgroup with MINI Kid diagnosis ($n=357$). Subjects less than 18 years old were included and there was no lower age limit.

Results: Attention-deficit/hyperactivity disorder (ADHD) symptoms significantly increased the odds for referral as social phobia symptoms significantly decreased the odds for psychiatric referral. Regarding quality of life (QoL), the control group showed significantly less impairment when compared with the referred group; the two referred subgroups with and without diagnosis did not differ significantly.

Conclusions: ADHD symptoms, even in a subthreshold level and impaired QoL represent risk factors for psychiatric referral in children. Secondary prevention of children should target to screen subthreshold ADHD symptoms and QoL.

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Child Psychiatry Hum Dev. 2013 Oct;44:678-88.

INCREASED PREFRONTAL OXYGENATION RELATED TO DISTRACTOR-RESISTANT WORKING MEMORY IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Tsujimoto S, Yasumura A, Yamashita Y, et al.

This study aimed at investigating the effect of distraction on working memory and its underlying neural mechanisms in children with attention-deficit/hyperactivity disorder (ADHD). To this end, we studied hemodynamic activity in the prefrontal cortex using near-infrared spectroscopy while 16 children with ADHD and 10 typically developing (TD) children performed a working memory task. This task had two conditions: one involved a distraction during the memory delay interval, whereas the other had no systematic distraction. The ADHD patients showed significantly poorer behavioral performance compared with the TD group, particularly under the distraction. The ADHD group exhibited significantly higher level of prefrontal activation than did TD children. The activity level was positively correlated with the severity of ADHD symptoms. These results suggest that the impairment in the inhibition of distraction is responsible for the working memory deficits observed in ADHD children. Inefficient processing in the prefrontal cortex appears to underlie such deficits.

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Clin Neurophysiol. 2013;124:2181-90.

ALTERED NEURAL CIRCUITS RELATED TO SUSTAINED ATTENTION AND EXECUTIVE CONTROL IN CHILDREN WITH ADHD: AN EVENT-RELATED FMRI STUDY.

Wang S, Yang Y, Xing W, et al.

Objective: The aim of this study was to investigate the neural basis of sustained attention, executive processing, and cognitive control in children with attention deficit hyperactivity disorder (ADHD).

Methods: Event-related functional magnetic resonance imaging (fMRI) was used to compare brain activation of 28 medication-naïve children with ADHD aged 7-12. years and 31 healthy controls during a cued continuous performance task (AX-CPT) in three stimulus context conditions (Go, NoGo, Lure).

Results: The children with ADHD showed increased activation in the left middle frontal gyrus, bilateral middle temporal gyrus, left precuneus and right cerebellum posterior lobe under the Lure condition compared to the controls. In the Lure condition, in contrast to the NoGo condition, an increased activation in the left inferior frontal gyrus, right medial frontal gyrus and right inferior parietal gyrus was observed in ADHD children.

Conclusions: The results demonstrate that medication-naïve ADHD children show spatial and temporal abnormalities in neural activities involved in sustained attention and executive control.

Significance: These findings show that there are distinct alternations in neural circuits related to sustained attention and executive control in children with ADHD, and further improve our understanding of the neural substrates of cognitive impairment in children with ADHD.

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Clin Psychol Rev. 2013.

DO PROGRAMS DESIGNED TO TRAIN WORKING MEMORY, OTHER EXECUTIVE FUNCTIONS, AND ATTENTION BENEFIT CHILDREN WITH ADHD? A META-ANALYTIC REVIEW OF COGNITIVE, ACADEMIC, AND BEHAVIORAL OUTCOMES.

Rapport MD, Orban SA, Kofler MJ, et al.

Children with ADHD are characterized frequently as possessing underdeveloped executive functions and sustained attentional abilities, and recent commercial claims suggest that computer-based cognitive training can remediate these impairments and provide significant and lasting improvement in their attention,

impulse control, social functioning, academic performance, and complex reasoning skills. The present review critically evaluates these claims through meta-analysis of 25 studies of facilitative intervention training (i.e., cognitive training) for children with ADHD. Random effects models corrected for publication bias and sampling error revealed that studies training short-term memory alone resulted in moderate magnitude improvements in short-term memory ($d = 0.63$), whereas training attention did not significantly improve attention and training mixed executive functions did not significantly improve the targeted executive functions (both nonsignificant: 95% confidence intervals include 0.0). Far transfer effects of cognitive training on academic functioning, blinded ratings of behavior (both nonsignificant), and cognitive tests ($d = 0.14$) were nonsignificant or negligible. Unblinded raters ($d = 0.48$) reported significantly larger benefits relative to blinded raters and objective tests (both $p < .05$), indicating the likelihood of Hawthorne effects. Critical examination of training targets revealed incongruence with empirical evidence regarding the specific executive functions that are (a) most impaired in ADHD, and (b) functionally related to the behavioral and academic outcomes these training programs are intended to ameliorate. Collectively, meta-analytic results indicate that claims regarding the academic, behavioral, and cognitive benefits associated with extant cognitive training programs are unsupported in ADHD. The methodological limitations of the current evidence base, however, leave open the possibility that cognitive training techniques designed to improve empirically documented executive function deficits may benefit children with ADHD.

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CNS Drugs. 2013;27:829-40.

HEALTH-RELATED QUALITY OF LIFE AND FUNCTIONAL OUTCOMES FROM A RANDOMIZED, CONTROLLED STUDY OF LISDEXAMFETAMINE DIMESYLATE IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Banaschewski T, Soutullo C, Lecendreux M, et al.

Background: Optimal management of attention deficit hyperactivity disorder (ADHD) aims not only to ameliorate patients' symptoms, but also to improve health-related quality of life (HRQL) and functioning. A pivotal, 7-week, randomized, double-blind, placebo-controlled, phase III study in children and adolescents in ten European countries demonstrated that the stimulant prodrug lisdexamfetamine dimesylate (LDX) is an effective and generally well-tolerated treatment for symptoms of ADHD.

Objective: The aim of this study was to assess HRQL and functional impairment outcomes in this clinical trial, using the Child Health and Illness Profile-Child Edition: Parent Report Form (CHIP-CE:PRF) and the Weiss Functional Impairment Rating Scale-Parent Report (WFIRS-P), respectively.

Methods: Patients (aged 6-17 years) with diagnosed ADHD and a baseline ADHD Rating Scale IV total score (greater-than or equal to)28 were randomized (1:1:1) to 7 weeks of double-blind treatment with once-daily LDX, placebo or the reference treatment, osmotic-release oral system methylphenidate (OROS-MPH). Participants' parents (or legally authorized representatives) completed the CHIP-CE:PRF and WFIRS-P questionnaires at baseline, at weeks 4 and 7, and/or at early termination. Endpoint was defined as the last on-treatment visit with valid data ((less-than or equal to)30 % missing items). The CHIP-CE:PRF Achievement domain was pre-specified as the primary HRQL outcome.

Results: The full analysis set comprised 317 patients (LDX, $n=104$; placebo, $n=106$; OROS-MPH, $n=107$), the majority of whom completed the study (LDX, $n=77$; placebo, $n=42$; OROS-MPH, $n=72$). Baseline CHIP-CE:PRF T-scores in four of the five domains were (greater-than or equal to)1 standard deviation below norms (US community samples). Compared with placebo, LDX was associated with statistically significantly improved T-scores from baseline to endpoint in these four domains, with effect sizes of 1.280 ($p<0.001$) in Achievement, 1.079 ($p<0.001$) in Risk Avoidance, 0.421 ($p<0.01$) in Resilience and 0.365 ($p<0.05$) in Satisfaction. In LDX-treated patients, placebo-adjusted improvements from baseline to endpoint in WFIRS-P scores were statistically significant ($p<0.001$) for total score and four of the six domains, with effect sizes of 0.924 (total score), 1.249 (Learning and School), 0.730 (Family), 0.643 (Social Activities) and 0.640 (Risky Activities). OROS-MPH treatment showed similar patterns of improvement from baseline to endpoint in both CHIP-CE:PRF and WFIRS-P scores.

Conclusions: Baseline HRQL and functional impairment scores reflect the burden of untreated ADHD. The benefits of short-term stimulant treatment in children and adolescents with ADHD extend beyond symptomatic relief and impact positively on HRQL and daily functioning.

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Cogn Behav Pract. 2013.

COMORBID ADHD: IMPLICATIONS FOR THE TREATMENT OF ANXIETY DISORDERS IN CHILDREN AND ADOLESCENTS.

Haldorsdottir T, Ollendick TH.

Despite high comorbidity rates and potential clinical implications, the influence of co-occurring attention-deficit/hyperactivity disorder (ADHD) on outcomes of cognitive-behavioral treatment (CBT) for anxious youth remains poorly understood. In this qualitative review, the current literature on the influence of comorbid ADHD on CBT of youth with diverse anxiety disorders is explored. Peer-reviewed studies examining ADHD, at the diagnostic and symptom level, received highest priority. In addition, inasmuch as some studies did not isolate the effects of ADHD from other disruptive behavior disorders (DBDs: oppositional defiant disorder, conduct disorders), studies with the three DBDs were explored as well. Ten studies met our specified methodological criteria. Findings are discussed in relation to the following two factors: type of anxiety disorder and measurement of ADHD (diagnostic or symptom level) in these studies. There was evidence that youth with a variety of anxiety disorders and with co-occurring ADHD fared worse than their counterparts without ADHD. Additionally, grouping ADHD with other DBDs tended to obscure the negative impact of ADHD on treatment outcomes. Additional research is needed to delineate the influence of comorbid ADHD specifically on treatment outcomes for the various anxiety disorders. Clinical implications of treating anxious youth with comorbid ADHD are explored.

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Drugs Context. 2013.

PHARMACOLOGICAL TREATMENT FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER: FUNCTIONAL OUTCOMES IN CHILDREN AND ADOLESCENTS FROM NON-WESTERN COUNTRIES.

Altin M, El-Shafei AA, Yu M, et al.

Objective: Functional outcomes were measured over a 12-month period in children and adolescents with attention deficit hyperactivity disorder (ADHD) after they received monotherapy.

Design: Prospective, observational, noninterventional study.

Setting: Conducted in six non-Western countries.

Participants: Outpatients 6 to 17 years of age with a verified diagnosis of ADHD in accordance with the Diagnostic and Statistical Manual, Fourth Edition, Text Revision (DSM-IV-TR), together with their physicians, decided to initiate or switch treatment for ADHD. Patients were prescribed pharmacological monotherapy: methylphenidate (n=221), nootropic agents (n=91), or atomoxetine (n=234).

Measurements: Patients were followed for changes in their functional status and quality of life, which were assessed with the Child Health and Illness Profile-Child Edition (CHIPCE) Achievement domain.

Results: At the end of the study, a mean improvement on the CHIP-CE Achievement domain score was observed for all countries and therapies except in Taiwan, where patients received atomoxetine, and in Lebanon, where patients received methylphenidate. No patient experienced a serious adverse event during the study. Four patients discontinued due to a treatment-emergent adverse event.

Conclusion: After 12 months of treatment, clinical and functional outcomes were improved in children and adolescents from non-Western countries who initiated and remained on their prescribed pharmacological monotherapy.

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Egypt J Med Hum Genet. 2013;14:383-89.

LANGUAGE IMPAIRMENT IN ATTENTION DEFICIT HYPERACTIVITY DISORDER IN PRESCHOOL CHILDREN.

El Sady SR, Nabeih AAS, Mostafa EMA, et al.

Language impairment (Li) is a highly prevalent comorbidity in children with psychiatric disorders and behavioral problems. The most common psychiatric diagnosis among children with Li is attention deficit hyperactivity disorder (ADHD), and conversely, Li is a frequent comorbidity found in children with ADHD. Despite the frequent cooccurrence of these two common disorders, there have been few studies that specifically investigate language abilities of children with ADHD. Therefore the main objective of this work was to evaluate language profile in ADHD children and to determine whether there is a specific ADHD related language profile in preschoolers in comparison with the control group with no ADHD. Fifty-three preschool children were diagnosed as ADHD and then they were evaluated for their language development. We recruited 36 children fulfilling our inclusion criteria and had delayed language development then we compared this case group to a sex and age matched group of children with delayed language with no ADHD (n=25). Assessment of intelligence was done for both groups using the Stanford Binnet Test IV. Evaluation of ADHD was done for both groups using DSM-IV criteria for ADHD. Comprehensive assessment of language development was done using the Arab Linguistic Test (ALT). EEG was done for both groups. Our results revealed that children with ADHD showed a significant delay in language development. But there was no difference between ADHD children and the control group in total language age, semantics, pragmatics and expressive language age. The only scale that showed difference between children with ADHD and controls was the receptive language age and receptive age quotient. There was no significant difference between cases and controls in EEG. We concluded that it is important to take into consideration language abilities when assessing children with ADHD and it is informative to include ADHD screening tools when dealing with children with DLD.

Emot Behav Difficulties. 2013;18:353-73.

CHILD AD/HD SEVERITY AND PSYCHOLOGICAL FUNCTIONING IN RELATION TO DIVORCE, REMARRIAGE, MULTIPLE TRANSITIONS AND THE QUALITY OF FAMILY RELATIONSHIPS.

Heckel L, Clarke AR, Barry RJ, et al.

Both Attention-Deficit/Hyperactivity Disorder (AD/HD) and divorce are very prevalent in western societies, and they may occur together. AD/HD is generally viewed as a neurobiological disorder, which has led to a commonly held belief that social-environmental factors play little role in the symptom profile of children diagnosed with the disorder. This study investigated the association between parental divorce, remarriage, multiple transitions, the quality of relationships with family members and the psychological well-being of children and adolescents with AD/HD. First, differences in children's AD/HD symptom profiles in relation to parents' divorce status (single/multiple divorce) and family composition (single parent/stepfamily) were examined. Second, the association between the quality of children's relationships with each family member and parents' marital status (divorced/non-divorced) and family composition was investigated. In addition, age, gender and AD/HD subtype differences were assessed. Third, the association between the quality of children's interactions with family members and children's AD/HD symptom profile was explored. No significant differences in children's behavioural profiles were found in terms of parents' divorce status. Living in stepfamilies was associated with greater AD/HD severity and social malfunctioning. Disruptive parent-child and sibling relationships were found to be related to children's age, gender, AD/HD subtype and parents' marital status. Further, poor interactions with family members correlated with children's AD/HD severity and psychological well-being. In summary, divorce, remarriage and the quality of relationships with family members are important correlates of the symptom profile of children with AD/HD, and this emphasises the need for special treatment modules for these families.

Epilepsia. 2013.

METHYLPHENIDATE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN YOUNG PEOPLE WITH LEARNING DISABILITY AND DIFFICULT-TO-TREAT EPILEPSY: EVIDENCE OF CLINICAL BENEFIT.

Fosi T, Lax-Pericall MT, Scott RC, et al.

Purpose: To establish the efficacy and safety of methylphenidate (MPH) treatment for attention deficit hyperactivity disorder (ADHD) in a group of children and young people with learning disability and severe epilepsy.

Methods: This retrospective study systematically reviewed the case notes of all patients treated with methylphenidate (MPH) for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) ADHD at a specialist epilepsy center between 1998 and 2005. Treatment efficacy was ascertained using clinical global impressions (CGI) scores, and safety was indexed by instances of >25% increase in monthly seizure count within 3 months of starting MPH.

Key Findings: Eighteen (18) patients were identified with refractory epilepsies (14 generalized, 4 focal), IQ <70, and ADHD. Male patients predominated (13:5) and ADHD was diagnosed at a median age of 11.5 years (range 6-18 years). With use of a combination of a behavioral management program and MPH 0.3-1 mg/kg/day, ADHD symptoms improved in 61% of patients (11/18; type A intraclass correlation coefficient of CGI 0.85, 95% confidence interval [CI] 0.69-0.94). Daily MPH dose, epilepsy variables, and psychiatric comorbidity did not relate to treatment response across the sample. MPH adverse effects led to treatment cessation in three patients (dysphoria in two, anxiety in one). There was no statistical evidence for a deterioration of seizure control in this group with the use of MPH.

Significance: Methylphenidate with behavioral management was associated with benefit in the management of ADHD in more than half of a group of children with severe epilepsy and additional cognitive impairments. Eighteen percent had significant side effects but no attributable increase in seizures. Methylphenidate is useful in this group and is likely to be under employed.

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Eur Child Adolesc Psychiatry. 2013;1-12.

ECONOMIC IMPACT OF CHILDHOOD/ADOLESCENT ADHD IN A EUROPEAN SETTING: THE NETHERLANDS AS A REFERENCE CASE.

Le HH, Hodgkins P, Postma MJ, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a highly prevalent psychiatric disorder in children/adolescents. This study reviews available European-based studies of ADHD-related costs and applies the findings to the Netherlands to estimate annual national costs for children/adolescents from a societal perspective. A systematic literature search was conducted for primary studies in Europe, published January 1, 1990 through April 23, 2013. Per-person cost estimates were converted to 2012 Euros and used to estimate annual national ADHD-related costs based on the Dutch 2011 census, ADHD prevalence rates, family composition, and employment rates. Seven studies met the inclusion criteria. The average total ADHD-related costs ranged from (euro)9,860 to (euro)14,483 per patient and annual national costs were between (euro)1,041 and (euro)1,529 million (M). The largest cost category was education ((euro)648 M), representing 62 and 42 % of the low- and high-value overall national estimates, respectively. By comparison, ADHD patient healthcare costs ranged between (euro)84 M (8 %) and (euro)377 M (25 %), and social services costs were (euro)4.3 M (0.3-0.4 %). While the majority of the costs were incurred by ADHD patients themselves, (euro)161 M (11-15 %) was healthcare costs to family members that were attributable to having an ADHD child/adolescent. In addition, productivity losses of family members were (euro)143-(euro)339 M (14-22 %). Despite uncertainties because of the small number of studies identified and the wide range in the national cost estimates, our results suggest that ADHD imposes a significant economic burden on multiple public sectors in Europe. The limited number of European-based studies examining the economic burden of ADHD highlights the need for more research in this area.

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Eur J Paediatr Neurol. 2013;17:S94.

NEUROFIBROMATOSIS TYPE 1: THE COMPLEX INTERPLAY OF COGNITION AND ATTENTION DEFICIT.

Lidzba K, Granstrom S, Krageloh-Mann I, et al.

Introduction: Attention Deficit with or without Hyperactivity (AD(H)D) is a common comorbidity of Neurofibromatosis Typ 1 (NF 1). While NF 1 is associated with problems in cognitive development, comorbid AD(H)D represents an additional risk factor. In this study, we tested the hypothesis that permanent medication with Methylphenidate can rescue cognitive problems in children with NF 1 and comorbid AD(H)D.

Patients and methods: We retrospectively analysed data of a clinical sample of patients with NF 1 with or without comorbid AD(H)D, who underwent standardized neuropsychological diagnostics twice (age range: T1 6-14 years; T2 7-16 years; mean interval 49.09 months). 16 children without AD(H)D were compared to 14 unmedicated children with AD(H)D and to 13 medicated children with AD(H)D. Effects of medication and attention on cognitive outcome (full-scale IQ) were tested by repeated measures analysis of covariance (rmANCOVA).

Results: We found a significant interaction between time and group, i.e., medicated children with NF 1 improved significantly in full-scale IQ from T1 to T2 (IQT1 = 80.38, IQT2 = 98.38, Cldiff: -25.59 to -10.40, $p < 0.0001$), this effect was not evident for the other groups. The interaction remained marginally significant when adding attention improvement as covariate.

Conclusion: Children and adolescents with NF 1 and comorbid AD(H)D may profit from MPH medication with respect to general cognition. As improvements in attention do not seem to be a strong source of this effect, this could be a specific feature of NF 1. Future prospective studies have to evaluate the mechanisms behind it.

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Eur J Paediatr Neurol. 2013;17:S93.

EFFECT OF RISK FACTORS ON CLINICAL AND ELECTROPHYSIOLOGICAL FINDINGS IN ADHD.

Kartal A, Aksoy E, Deda G.

Objectives: Attention deficit hyperactivity disorder (ADHD) is one of the most commonly seen developmental disorders in childhood. It's etiology however is not well known even though bio-psycho-social reasons have been thought to play a big role. In this retrospective study, the risk factors of ADHD are identified in patients diagnosed with ADHD in childhood; and the aim of the study was to analyse the relationship between clinical symptoms and risk factors to which they were exposed to and their effects on the electrophysiological findings.

Material and methods: In this study, the records of 310 patients between 6-15 years of age diagnosed as ADHD who were followed up between January 2007 to May 2012 at Ankara University Medical School Pediatric Neurology and Psychiatry departments were studied retrospectively. Out of 310 patients only 140 met the study criteria and were included in the study. The exclusion criteria were as follows; IQ levels below 80, patients with chronic diseases, patients with pervasive developmental disorders or psychotic disorders and syndromic patients.

Results: The mean age of the subjects was 9.25 (plus or minus) 2.02, 119 (85%) were boys, and 21 (13.6%) girls. Epileptiform abnormalities in EEG were found in 32 (22.9%) patients, discharges were mostly in the centrottemporal, parietooccipital, and frontal area. A previous history of epileptic seizures was reported in 20 (14.3%) patients. ADHD- inattentive type was the most common subtype of ADHD.

Conclusion: In our study, asphyxia was found to have an effect on the incidence of epilepsy, and gestational age, asphyxia were found to have an effect on the incidence of epileptiform activity.

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Eur J Paediatr Neurol. 2013;17:S27.

EFFECTS OF METHYLPHENIDATE ON FUNCTIONAL NETWORKS ACTIVATION IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Berquin P, Querne L, Service De Fall S, et al.

Background: Many fMRI studies in ADHD had focused on frontal regions known to be a site of action of methylphenidate and be involved in executive, control and inhibitory functions. New approach shifts the focus from regional brain abnormalities to dysfunction in distributed network organization. The objective was to study how the methylphenidate modifies in children with ADHD the activations of functional networks during visuospatial processing.

Methods: Eleven drug-naive ADHD children and 11 typically developing (TD) children performed a flanker task during magnetic resonance imaging. The ADHD-group was scanned twice, before initiation of methylphenidate and one month afterwards with methylphenidate (extended-release formulation). The functional sequence consisted of successive conflict/ unconflicting blocks. Brain activity for visuomotor conflict was imaged by contrasting hemodynamic activity during conflict versus unconflicting blocks.

Results: Prior to methylphenidate, the ADH-group showed bilateral activations in visual and dorsalattentional (only the posterior part) networks and in several regions of the default-mode network. In contrast, the TD-group showed bilateral activation in the fronto-parietal network. With methylphenidate, activations in the ADHD-group were reduced in both visual and default-mode networks. Methylphenidate also initiated activations in the anterior part of the dorsalattentional network and in the right hemispheric part of the fronto-parietal network.

Conclusions: Our results suggest that ADHD children engaged different networks than TD children for performed visuomotor conflict. Hyperactivation of the visual, dorsal-attentional and default- mode networks could be compensatory mechanisms and/or be consecutive to a default of inhibitory control normally exerted by the fronto-parietal network. Methylphenidate by improving partially the activation of the fronto-parietal network may improve in turn inhibitory control on visual and default-mode networks. The dorsal attentional network remained activated, suggesting that attentional networks compensate the incomplete activation of the frontoparietal network.

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Eur J Paediatr Neurol. 2013;17:S26.

DO ROLANDIC SPIKES ON EEG AT ADHD ASSESSMENT INFLUENCE ON ADHD SUBTYPE AND THE USE OF METHYLPHENIDATE FOR ADHD?

Socanski D, Herigstad A.

There are some relationships between attention-deficit/hyperactivity disorder (ADHD) and rolandic spikes (RS) on EEG. RS occur in children with ADHD and may contribute to the occurrence of ADHD symptoms in some cases.

Purpose: The aim of the present study was to investigate whether RS on EEG at ADHD assessment influence on the occurrence of ADHD subtype and the use of methylphenidate (MPH) for ADHD.

Method: A retrospective study of 607 ADHD children (82.4% male), aged between 5 and 14 years, who were diagnosed between January 2000 and December 2005 was performed. At least one routine awake EEG was recorded on 517 patients and 39 patients had EEG with epileptiform abnormalities (EA). The group with RS (group one) was compared to control groups; group two (patients with EA without RS) and group three (patients without EA). The three groups were followed-up for one year.

Measure outcomes were: ADHD subtype and the use of MPH for ADHD.

Results: The group with RS consisted of 9 patients, 2 of them had previous history of epilepsy. Group two (patients with EA without RS), consisted of 30 patients, 10 of them had previous epilepsy. Of the 30 patients without EA (group three), nobody had previous epilepsy. ADHD combined subtype was diagnosed in the vast majority of cases in all groups. MPH was used similarly in groups (89%, group one; 87%, group two; 83%, group three). There was no statistic difference between groups with and without RS where MPH was used as medication for ADHD. The previous epilepsy co-morbidity and occurrence of RSs were not a reason for not treating ADHD.

Conclusions: The study suggested that RS occurrence at ADHD assessment does not influence on ADHD subtype occurrence and the use of MPH during 12 months follow-up.

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Eur J Paediatr Neurol. 2013;17:S73.

ATTENTION DEFICIT AND THE ASSOCIATED CLINICAL FACTORS IN CHILDREN WITH BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES (BCECTS).

Kim EH, Yum MS, Kim HW, et al.

Objectives: Children with epilepsy often experience attentional problems with less favorable outcomes. We assessed the attention in benign childhood epilepsy with centro-temporal spikes (BCECTS) and tried to identify the associated seizure variables which cause attentional problems.

Material and methods: A total of 266 children were diagnosed with BCECTS at Asan Medical Center from 2004 to 2012. Among them, 93 children (57 males) who performed the formal attention test (ATA or CAT) were retrospectively reviewed. Clinical data including sex, age of seizure onset, seizure control, EEG findings, and response to treatment were analyzed to evaluate the association with attention deficit.

Results: A mean age of seizure onset was 7.5 (3.3-13.3) years and mean follow-up duration after diagnosis was 3.4 (1-8.7) years. Of 93 patients, 63 (67.7%) were diagnosed as having attention deficit, including the inattentive type (32 cases, 50.8%) and the combined type (25 cases, 39.7%). The incidence of attention deficit was significantly higher in children with a younger age of seizure onset (86.5% [3-6 years] vs 55.4% [7-14 years], $p=0.02$). However, other clinical factors, frequency and laterality of spike discharges on electroencephalogram (EEG), duration of treatment, seizure control were not associated with the incidence of attention deficit. And there was no factor related to attention quotient of visual or auditory selection. Eighteen patients (28.5%) were treated with central nervous system stimulants, and their epilepsy related factors and outcome were similar with those of patients without stimulant medication. There was no case with aggravated seizure after stimulants.

Conclusions: Children with BCECTS have a high incidence of attention deficit and early onset of seizure was associated with this attention deficit. Therefore, systematic screening and proper management for attentional problems should be carried out in these patients.

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Eur J Paediatr Neurol. 2013;17:S25.

MOTOR CORTICAL INHIBITION IN ADHD: MODULATION OF THE TRANSCRANIALMAGNETIC STIMULATION-EVOKED N100 DURING A GO/NOGO TASK.

D'Agati E, Hoegl T, Dippel G, et al.

Objectives: The N100 component, evoked by transcranial magnetic stimulation (TMS) and electroencephalography (EEG) is associated with the activation of inhibitory cortical circuits and has recently been suggested as a potential marker of inhibition in Attention Deficit Hyperactivity Disorder (ADHD). In healthy subjects, the TMS-evoked N100 decreases during motor response preparation and movement execution and increases during response inhibition. This study is the first investigating modulation of the TMS-evoked N100 at stages of response preparation, activation, execution and inhibition in ADHD patients during a go/nogo task. The aim of the present study was to investigate the modulation of the TMS-evoked N100 at stages.

Material and methods: 18 children with ADHD and 19 typically developing children, aged 10 to 14 years, all right handed were assessed. TMS was delivered over the left motor cortex, the TMS-N100 was measured at electrode P3. The TMS-evoked N100 was determined at rest and at different time points (50 ms before S2; 150, 300 and 500 ms after S2) in a cued go/nogo task (S1-S2 paradigm). Correlations between the TMS-evoked N100 measures, MEP-related TMS measures (e.g., short-interval intracortical inhibition) and performance measures were calculated.

Results: Though the TMS-evoked N100 was not found to be significantly reduced at rest in the ADHD group, a smaller increase in go trials and a smaller decrease after inhibiting a response compared to

typically developing children were observed. In go trials, a lower TMS-evoked N100 was associated with a smaller variability of reaction times.

Conclusions: A reduced modulation of the TMS-evoked N100 amplitude at response execution and inhibition during a go/nogo task, extends the picture of inhibition deficits at the cortical level in ADHD underlining the relevance of the TMS-evoked N100. Findings suggest a functional involvement of the mechanisms underlying the TMS-evoked N100 at the motor output stage.

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Eur J Paediatr Neurol. 2013;17:S95.

EFFECTS OF METHYLPHENIDATE ON DEFAULT-MODE NETWORK/TASK-POSITIVE NETWORK SYNCHRONIZATION IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY.

Querne L, Fall S, Le Moing AG, et al.

Background: A failure of the anti-phase synchronization between the default-mode network (DMN) and the task-positive network (TPN) may be involved in one of the main manifestations of attention deficit hyperactivity disorder (ADHD): moment-to-moment variability. Although methylphenidate reduces response time (RT) variability during tasks and increases DMN deactivation, it is not clear whether methylphenidate affects TPN/DMN synchronization. The present study investigated temporal aspects of hemodynamic activity in order to test the hypothesis whereby methylphenidate may improve TPN/DMN synchronization in children with ADHD.

Methods: Eleven drug-naïve ADHD children and 11 typically developing (TD) children performed a flanker task during magnetic resonance imaging. The ADHD group was scanned twice, before initiation of methylphenidate and one month afterwards with methylphenidate (extended-release formulation). The blood-oxygen-level-dependent signal was analyzed by independent component analysis. Components involving the DMN were sought.

Results: As expected, TD group showed anti-phase synchronization between the DMN and TPN during the flanker task. Prior to initiation of medication, the ADHD group showed synchronous activity in posterior regions of the DMN only. This component was positively correlated with RT variability during the flanker task. Methylphenidate partially restored anti-phase synchronization in the TPN/DMN complex, reduced RT variability during the task and abolished the correlation between RT variability and DMN activity.

Conclusions: Our results suggest that a failure of the TPN/DMN synchronization is involved in the moment-to-moment variability displayed by children with ADHD. Methylphenidate initiated TPN/DMN synchronization, which in turn appeared to reduce moment-to-moment variability during goal-directed tasks.

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Eur J Paediatr Neurol. 2013;17:S94.

How ADHD SYMPTOMS CAN BE MODULATED BY IMMEDIATE ENVIRONMENT MODIFICATIONS?

Baijot S, Deconinck N, Slama H, et al.

Objective: Recent research has found that adapted noise can be beneficial for the nervous system (Moss et al. 2004). Noise benefits have been validated for several cognitive tasks like arithmetic, visual signals detection. In ADHD, an adapted level of noise has been suggested to compensate for the hypofunction of dopamine transmission (Solanto, 2002). For instance, it has been found that noise during an episodic memory task improved ADHD children's performance (Sikstrom & Soderlund, 2007). The objective of this ongoing study is to assess the potential benefits of noise, in ADHD compared to typically developing children (TDC), using both behavioral and neurophysiological measures (ERPs) during a neuropsychological task.

Method: Nine ADHD children (mean age = 9; SD = 1) and 16 TDC (mean age = 9.1; SD = 1.3) performed a visual Cued Go/Nogo (adapted from Smith et Johnstone, 2006) across two conditions (noise and no-noise exposure). ADHD children stopped medication 24 hours before testing. ANOVAs were performed on Go (correct responses) and false alarms associated with impulsivity.

Results: ADHD children committed more false alarms than TDC ($p=0.05$). A significant interaction Group null Noise ($p=0.009$) indicated a difference between groups in the no-noise condition ($p=0.01$) but no difference when ADHD listened to the noise ($p=0.96$). In addition, ADHD children had less Go responses than TDC ($p=0.004$). A marginal interaction Group null Noise ($p=0.08$) indicated a difference between groups in the no-noise condition ($p=.005$) but no difference when ADHD listened to the noise ($p=0.18$).

Conclusion: Our first preliminary results are congruent with our hypothesis. ADHD children did benefit from noise during executive task. They improved their performance as regards to both correct responses and false alarms. Group differences disappeared during white noise exposure, mainly due to ADHD group improvements rather than impairments by the control group.

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Eur J Pediatr. 2013;1.

MORE AND BETTER SHOULD BE DONE TO GUARANTEE EVIDENCE-BASED MANAGEMENT OF ADHD IN CHILDREN ACROSS EUROPE.

Reale L, Clavenna A, Panei P, et al.

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Exp Clin Psychopharmacol. 2013 Oct;21:385-407.

MISUSE OF PRESCRIPTION STIMULANTS AMONG COLLEGE STUDENTS: A REVIEW OF THE LITERATURE AND IMPLICATIONS FOR MORPHOLOGICAL AND COGNITIVE EFFECTS ON BRAIN FUNCTIONING.

Weyandt LL, Marraccini ME, Gudmundsdottir BG, et al.

Prescription stimulant medication, the most frequently recommended treatment for college students with attention deficit/hyperactivity disorder (ADHD), has become increasingly available on college campuses. Research investigating prescription stimulant misuse among college students indicates that significant numbers of students without ADHD are taking prescription stimulants to enhance their cognitive performance. This article systematically reviews studies concerning misuse of prescription stimulants among college students with and without ADHD as well as the cognitive and morphological brain changes associated with prescription stimulants in humans and other animals. Whether these morphological changes are accompanied by improved cognitive performance remains equivocal. Implications of this body of literature are discussed and suggestions for future research are advanced.

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Farmacia. 2013;61:1000-08.

PHARMACOLOGICAL TREATMENT IN STABILIZING THE SYMPTOMS IN CHILDREN WITH ADHD SYMPTOMS.

Toufic Seblany H, Stefania Dinu I, Safer M, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a chronic disorder characterized by problems with paying attention, impulsivity and over-activity which influence all the life fields of a child with ADHD. The prevalence of ADHD in children is approximately 7% worldwide, both males and females being affected and with different etiology. A high rate of these patients present neurologic etiology, determined by factors which occurred in different stages of the development process. The consequences of ADHD cause social problems because these children have difficulties regarding family, school and social integration, associating a considerable impairment in the quality of life (QoL). The goal of therapeutic approaches is to improve the QoL by managing the symptoms. There is no treatment for curing ADHD, but there is a pharmacologic treatment used in order to control the symptoms. The goal of the study was to determine the impact of treatment on symptoms control in ADHD patients. The subjects were administered methylphenidate or atomoxetine. The ADHD symptoms were screened with Child Symptom Inventory-4 scale. Pharmacological treatment and early diagnosis have a positive impact on outcomes, QoL and long-term prognosis.

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Hum Brain Mapp. 2013.

PATTERN CLASSIFICATION OF RESPONSE INHIBITION IN ADHD: TOWARD THE DEVELOPMENT OF NEUROBIOLOGICAL MARKERS FOR ADHD.

Hart H, Chantiluke K, Cubillo AI, et al.

The diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) is based on subjective measures despite evidence for multisystemic structural and functional deficits. ADHD patients have consistent neurofunctional deficits in motor response inhibition. The aim of this study was to apply pattern classification to task-based functional magnetic resonance imaging (fMRI) of inhibition, to accurately predict the diagnostic status of ADHD. Thirty adolescent ADHD and thirty age-matched healthy boys underwent fMRI while performing a Stop task. fMRI data were analyzed with Gaussian process classifiers (GPC), a machine learning approach, to predict individual ADHD diagnosis based on task-based activation patterns. Traditional univariate case-control analyses were also performed to replicate previous findings in a relatively large dataset. The pattern of brain activation correctly classified up to 90% of patients and 63% of controls, achieving an overall classification accuracy of 77%. The regions of the discriminative network most predictive of controls included later developing lateral prefrontal, striatal, and temporo-parietal areas that mediate inhibition, while regions most predictive of ADHD were in earlier developing ventromedial fronto-limbic regions, which furthermore correlated with symptom severity. Univariate analysis showed reduced activation in ADHD in bilateral ventrolateral prefrontal, striatal, and temporo-parietal regions that overlapped with areas predictive of controls, suggesting the latter are dysfunctional areas in ADHD. We show that significant individual classification of ADHD patients of 77% can be achieved using whole brain pattern analysis of task-based fMRI inhibition data, suggesting that multivariate pattern recognition analyses of inhibition networks can provide objective diagnostic neuroimaging biomarkers of ADHD.

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Indian J Physiol Pharmacol. 2013;57:270-79.

REGION-WISE GRAY MATTER VOLUME ALTERATIONS IN BRAIN OF ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVE DISORDER: A VOXEL BASED MORPHOMETRIC ANALYSIS.

Ramesh MG, Rai KS.

Attention Deficit Hyperactive Disorder (ADHD) is a behavioral neuropsychiatric disorder affecting an estimated 5% of school-age children worldwide with symptoms persisting into adulthood in 80% of cases. Presently clinical diagnosis and treatment of ADHD relies on behavioral disturbances than on detecting underlying defective brain regions. Therapeutic outcome in treatment of ADHD may be more positive if defective brain region in clinically diagnosed ADHD is detected by voxel based morphometric (VBM) analysis that measures voxel-wise global and regional focal volume differences in structural magnetic resonance images (sMRI) of brain. This study was designed to detect any region-specific gray matter (GM) volume defects in sMRI of ADHD adolescents by VBM analysis. Thirty sMRI datasets matched for sex, handedness of adolescents aged between 11.66 and 20.47 years (mean age 16.27(plus or minus)2.48 years) obtained from NeuroImage webpage, were selected (Control n=15; ADHD combined type n=15). These sMRI were analyzed by VBM technique and compared using statistical parametric mapping (SPM). Significant regional GM volume deficits ($P < 0.05$) was specifically identified in left cuneus and middle occipital gyrus in ADHD, after voxel-wise false discovery rate correction over the whole brain compared to matched controls. Deficit of GM volume in occipital cortex detected by VBM analysis in ADHD children, suggests defects of visual processing affecting attention mechanisms.

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Int J Hum Gen. 2013;13:145-52.

THE CORRELATION OF ATTENTION DEFICIT HYPERACTIVITY DISORDER WITH DRD4 GENE POLYMORPHISM IN TURKEY.

Guney E, Iseri E, Ergun SG, et al.

Attention Deficit Hyperactivity Disorder (ADHD) is a disorder with a strong genetic background, and genetic factors are thought to play a crucial role in its aetiology and developmental course. In this study the researchers investigated the correlation of ADHD with the dopamine receptor D4 (DRD4) gene. Fifty patients (6-10 years of age) diagnosed between 1994 and 2001 and followed up 7-14 years until their adolescence and young adulthood (16-25 years of age) were included in the study. Fifty healthy individuals of the same age were included as the control group. DRD4 gene analysis of patients was performed after detailed clinical evaluation. The researchers found that 88% of patients continued to meet the criteria of ADHD in adolescence and young adulthood. The most frequent DRD4 gene alleles among the ADHD and control groups were 4-, 8-and 2-repeat alleles. While the frequency of the 8-repeat allele was higher than reported global estimations, none of the three alleles were found to be significant for ADHD. However, in the presence of the 2-repeat allele for the combined subtype of ADHD diagnosed in childhood, the persistence ratio was found to be statistically significant in adolescence and young adulthood. The DRD4 gene may play a role in the developmental course of ADHD in the Turkish population.

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Int J Psychophysiol. 2013;89:314-19.

EXCESS BETA ACTIVITY IN THE EEG OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A DISORDER OF AROUSAL?

Clarke AR, Barry RJ, Dupuy FE, et al.

Past research has reported that a small proportion of children with attention-deficit/hyperactivity disorder (AD/HD) have excess beta activity in their EEG, rather than the excess theta typical of the syndrome. This atypical group has been tentatively labeled as hyperaroused. The aim of this study was to determine whether these children have a hyperaroused central nervous system. Participants included 104 boys aged 8 to 13. years old, with a diagnosis of either the Combined or Inattentive type of AD/HD (67 combined type), and 67 age-matched male controls. Ten and a half minutes of EEG and skin conductance (SCL) were simultaneously recorded during an eyes-closed resting condition. The EEG was Fourier transformed and estimates of total power, and relative power in the delta, theta, alpha, and beta bands, and the theta/beta ratio, were calculated. AD/HD patients were divided into an excess beta group and a typical excess theta group. Relative to controls, the typical excess theta group had significantly increased frontal total power, theta and theta/beta ratio, with reduced alpha and beta across the scalp. The excess beta group had significantly reduced posterior total power, increased centro-posterior delta, globally reduced alpha, globally increased beta activity, and globally reduced theta/beta ratio. Both AD/HD groups had significantly reduced SCL compared to the control group, but the two groups did not differ from each other on SCL. These results indicate that AD/HD children with excess beta activity are not hyperaroused, and confirm that the theta/beta ratio is not associated with arousal. This is the first study of arousal measures in AD/HD children with excess beta activity, and has implications for existing models of AD/HD.

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Int J Psychophysiol. 2013;89:320-27.

SEX DIFFERENCES BETWEEN THE COMBINED AND INATTENTIVE TYPES OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: AN EEG PERSPECTIVE.

Dupuy FE, Barry RJ, Clarke AR, et al.

This study investigated sex differences between the EEGs of Combined and Inattentive types of attention-deficit/hyperactivity disorder (AD/HD) within boys and girls aged 8-12. years. Subject groups included 80. AD/HD Combined type (40 boys and 40 girls), 80. AD/HD Inattentive type (40 boys and 40 girls) and 80 controls (40 boys and 40 girls). An eyes-closed resting EEG was recorded and Fourier transformed to provide estimates for absolute and relative power in the delta, theta, alpha and beta frequency bands, as

well as total power and the theta/beta ratio. The boy AD/HD groups, compared with boy controls, had greater absolute and relative theta, greater theta/beta ratio, reduced absolute and relative alpha, and reduced absolute and relative beta. The girl AD/HD groups, compared with girl controls, had greater absolute delta, greater absolute and relative theta, greater theta/beta ratio, greater total power, and reduced relative delta and relative beta. Between AD/HD types, Combined type boys had globally greater absolute and relative theta, greater theta/beta ratio, and less relative alpha than Inattentive type boys. While topographical differences emerged, there were no significant global differences between AD/HD types in girls. That is, EEG differences between AD/HD types are dissimilar in boys and girls. Different EEG maturational patterns between boys and girls also obscure AD/HD-related EEG abnormalities. These results have important implications for our understanding of AD/HD in girls. Ignoring such sex differences may have compromised the value of previous AD/HD investigations, and these sex differences should be recognised in future research.

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J Abnorm Child Psychol. 2013 Oct;41:1161-75.

CONTINUITIES AND CHANGES IN THE FRIENDSHIPS OF CHILDREN WITH AND WITHOUT ADHD: A LONGITUDINAL, OBSERVATIONAL STUDY.

Normand S, Schneider BH, Lee MD, et al.

We examined how the real-life dyadic friendships of 87 children with ADHD and 46 comparison children (76 % boys) aged 7–13 years evolved during a 6-month follow-up period. The methods included friendship quality self-report measures and direct observation of friends' dyadic behaviors in three structured analogue tasks. At Time 2, the friends of the participants with ADHD reported less positive friendship quality and more conflict with their friends than at Time 1. They were also considerably less satisfied with their friendship than 6 months prior. In contrast, the friends of comparison children reported fewer negative friendship features, more positive friendship features and a slightly greater friendship satisfaction than at Time 1. In sharp contrast with the invited friends' reports, referred children with ADHD did not report deterioration in their friendship quality over time. Unlike comparison children who significantly reduced violations of game rules between Time 1 and Time 2, children with ADHD broke more game rules during the same period. In negotiating with friends, comparison children, but not children with ADHD, reduced the number of self-centered and insensitive proposals at Time 2. Controlling for Time 1 variance, violations of game rules and a self-centered, insensitive negotiation approach predicted deterioration in friendship quality for children with and without ADHD over time.

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J Abnorm Child Psychol. 2013 Oct;41:1145-59.

WHAT SPECIFIC FACETS OF EXECUTIVE FUNCTION ARE ASSOCIATED WITH ACADEMIC FUNCTIONING IN YOUTH WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER?

Langberg JM, Dvorsky MR, Evans SW.

The purpose of the study was to evaluate the relation between ratings of Executive Function (EF) and academic functioning in a sample of 94 middle-school-aged youth with Attention-Deficit/Hyperactivity Disorder (ADHD; Mage =11.9; 78 % male; 21 % minority). This study builds on prior work by evaluating associations between multiple specific aspects of EF (e.g., working memory, inhibition, and planning and organization) as rated by both parents and teachers on the Behavior Rating Inventory of Executive Function (BRIEF), with multiple academic outcomes, including school grades and homework problems. Further, this study examined the relationship between EF and academic outcomes above and beyond ADHD symptoms and controlled for a number of potentially important covariates, including intelligence and achievement scores. The EF Planning and Organization subscale as rated by both parents and teachers predicted school grades above and beyond symptoms of ADHD and relevant covariates. Parent ratings of youth's ability to transition effectively between tasks/situations (Shift subscale) also predicted school grades. Parent-rated symptoms of inattention, hyperactivity/impulsivity, and planning and organization abilities were significant in the final model predicting homework problems. In contrast, only symptoms of

inattention and the Organization of Materials subscale from the BRIEF were significant in the teacher model predicting homework problems. Organization and planning abilities are highly important aspects academic functioning for middle-school-aged youth with ADHD. Implications of these findings for the measurement of EF, and organization and planning abilities in particular, are discussed along with potential implications for intervention.

J Abnorm Psychol. 2013 Aug;122:842-53.

DOES LOW BIRTH WEIGHT SHARE COMMON GENETIC OR ENVIRONMENTAL RISK WITH CHILDHOOD DISRUPTIVE DISORDERS?

Ficks C, Lahey BB, Waldman ID.

Although advances in neonatal care over the past century have resulted in increased rates of survival among at-risk births, including infants with low birth weight, we have much to learn about psychological outcomes in this population. In particular, despite growing evidence that low birth weight may be associated with an increased risk for Attention-Deficit/Hyperactive Disorder (ADHD) symptoms in childhood, few studies have examined birth weight as a risk factor for disruptive disorders that commonly co-occur with ADHD. In addition, the etiology of the relation between birth weight and these disorders is unknown. The current investigation aimed to better understand these associations in the context of potentially confounding genetic and environmental influences by examining phenotypic associations between birth weight and disruptive disorder symptoms both between families and within families in two independent twin samples (Sample 1: N = 1,676 individuals; Sample 2: N = 4,038 individuals). We found negative associations between birth weight and inattentive, hyperactive-impulsive, and broad externalizing symptoms in both samples. Nonetheless, the overall magnitude of these associations was very small, contributing to less than 1% of the variance in these symptom dimensions. Within-family associations between birth weight and disruptive disorder symptoms did not differ for monozygotic and dizygotic twin pairs, suggesting that nonshared environmental influences rather than common genetic influences are responsible for these associations. Overall, the consistent albeit weak associations between birth weight and disruptive disorder symptoms suggest that low birth weight may not represent a major risk factor in the development of these symptoms.

J Affective Disord. 2013.

RE-EXAMINING THE RISK FOR SWITCH FROM UNIPOLAR TO BIPOLAR MAJOR DEPRESSIVE DISORDER IN YOUTH WITH ADHD: A LONG TERM PROSPECTIVE LONGITUDINAL CONTROLLED STUDY.

Biederman J, Wozniak J, Tarko L, et al.

Background: Recent studies have identified subthreshold forms of bipolar (BP)-I disorder and deficits in emotional regulation as risk factors for bipolar disorder in youth. The primary aim of this study was to investigate whether emotional dysregulation and subthreshold forms of BP-I disorder increase the risk for BP switches in ADHD youth with non-bipolar MDD.

Methods: We used data from two large controlled longitudinal family studies of boys and girls with and without ADHD. Subjects (N=522) were followed prospectively and blindly over an average follow up period of 11.4 years. Comparisons were made between ADHD youth with unipolar major depression (MDD) who did (N=24) and did not (N=79) switch to BP-I disorder at follow-up.

Results: The rate of conversion to BP-I disorder at follow up was higher in MDD subjects with subthreshold BP-I disorder at baseline compared to those without (57% vs. 21%; OR=9.57, 95% CI=1.62-56.56, p=0.013) and in MDD subjects with deficient emotional self-regulation (OR=3.54, 95% CI=1.08-11.60, p=0.037).

Limitations: The sample was largely Caucasian, so these results may not generalize to minority groups. The sample of youth with SED was small, which limited the statistical power for some analyses.

Conclusions: Switches from unipolar MDD to BP-I disorder in children with ADHD and MDD were predicted by baseline subthreshold BP-I disorder symptoms and baseline deficits in emotional regulation. More work is needed to assess whether these risk factors are operant outside the context of ADHD.

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Journal of Applied Behavior Analysis. 2013;46:695-98.

THE EFFECTS OF AWARENESS TRAINING ON TICS IN A YOUNG BOY WITH TOURETTE SYNDROME, ASPERGER SYNDROME, AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Wiskow KM, Klatt KP.

Previous research has shown habit reversal training (HRT) to be effective in reducing tics. In some studies, tics have been reduced by implementing only a few components of HRT. The current study investigated the first step, awareness training, for treating tics in a young boy with Asperger syndrome, Tourette syndrome, and attention deficit hyperactivity disorder. The results showed a reduction in all tics.

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J Child Adolesc Psychopharmacol. 2013;23:448-57.

EFFECTS OF NEUROFEEDBACK VERSUS STIMULANT MEDICATION IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A RANDOMIZED PILOT STUDY.

Ogrim G, Hestad KA.

Objective: The purpose of this pilot study was to compare the effects of 30 sessions of neurofeedback (NF) with stimulant medication on attention-deficit/hyperactivity disorder (ADHD) patients.

Methods: Thirty-two medication-naïve ADHD patients, ages 7-16, from a neuropsychiatric clinic, were randomized to NF (n=16) or drug treatment (n=16). Other actions, such as parent management training, information, or support in school were given as needed, with no differences between the groups. All participants were assessed before treatment on two rating scales, each with parent and teacher forms. In addition, quantitative electroencephalogram (QEEG) and event-related potentials (ERPs), which included behavioral data from a go/no go test were administered. NF training took place in the clinic over a period of 7-11 months, and was followed by a repeat of the same assessment tools. The mean time interval between pre- and postassessment was not significantly different in the two groups. The 18 symptoms of ADHD (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV)) were used as the primary outcome measure.

Results: Analysis of covariance revealed a significant difference between the groups at evaluation in favor of medication, with a large effect size. This picture was confirmed by other outcome measures. The QEEG spectral power in the theta and beta bands did not change in either group. In ERP, the P3 no go component increased significantly in 8 of 12 patients who had a clinically relevant medication effect, but did not increase in the medication nonresponders or the NF group.

Conclusions: Our study supports effects for stimulants, but not for NF. Effects of NF may require thorough patient selection, frequent training sessions, a system for excluding nonresponders, and active transfer training. The P3 no go ERP component may be a marker for treatment response.

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J Clin Neurol. 2013;26:47-48.

CHANGE OF ELECTROENCEPHALOGRAPHY IN CHILDREN WITH VARIOUS TYPE OF ATTENTION-DEFICIT-HYPERACTIVITY DISORDER.

Chen X.

Objective: To investigate the change of electroencephalography (EEG) in children with various type of attention-deficit-hyperactivity disorder (ADHD).

Method: EEG was examined in 152 children whose clinical diagnosed ADHD. Integrated visual and auditory continuous performance test (IVA-CPT) was performed in ADHD children for ADHD typing. The change of EEG were analyzed in the different ADHD type children.

Results: In this group, normal EEG was in 108 cases (71. 1%), abnormal EEG in 44 cases (28. 9%); all of the abnormal EEG was nonspecific. IVA-CPT was showed normal in 18 cases (11. 8%), predominantly inattentive type in 41 cases (27. 0%), predominantly hyperactive-impulsive type in 27 cases (17. 8%), combined type in 40 cases (26. 3%), and hyperactive invalid in 26 cases (17. 1%). The abnormal rate of EEG in predominantly inattentive type was 25.0%, predominantly hyperactive/impulsive type was 18. 2% and combined type was 18. 2%; and the rates of abnormal EEG was no statistical significance among each ADHD types.

Conclusions: There is no particular EEG change in ADHD children. The rates of abnormal EEG in different ADHD types are basically similar.

J Consult Clin Psychol. 2013;81:918-25.

DEVELOPMENT AND PRELIMINARY EVALUATION OF AN INTEGRATED TREATMENT TARGETING PARENTING AND DEPRESSIVE SYMPTOMS IN MOTHERS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Chronis-Tuscano A, Clarke TL, O'Brien KA, et al.

Objective: More than 50% of mothers of children with attention-deficit/ hyperactivity disorder (ADHD) have a lifetime history of major depressive disorder (MDD). Maternal depressive symptoms are associated with impaired parenting and predict adverse developmental and treatment outcomes for children with ADHD. For these reasons, we developed and examined the preliminary efficacy of an integrated treatment targeting parenting and depressive symptoms for mothers of children with ADHD. This integrated intervention incorporated elements of 2 evidence-based treatments: behavioral parent training (BPT) and cognitive behavioral depression treatment.

Method: Ninety-eight mothers with at least mild depressive symptoms were randomized to receive either standard BPT (n = 51) or the integrated parenting intervention for ADHD (IPI-A; n = 47). Participants were assessed at baseline, posttreatment, and 3- to 6-month follow-up on measures of (a) self-reported maternal depressive symptoms, (b) observed positive and negative parenting, and (c) observed and mother-reported child disruptive behavior and mother-reported child and family impairment.

Results: The IPI-A produced effects of small to moderate magnitude relative to BPT on maternal depressive symptoms, observed negative parenting, observed child deviance, and child impairment at posttreatment and on maternal depressive symptoms, child disruptive behavior, child impairment and family functioning at follow-up. Contrary to expectations, the BPT group demonstrated moderate to large effects relative to IPI-A on observed positive parenting at follow-up.

Conclusions: This treatment development study provides encouraging preliminary support for the integrated intervention targeting parenting and depressive symptoms in mothers of children with ADHD. Future studies should examine whether this integrated intervention improves long-term developmental outcomes for children with ADHD.

J Consult Clin Psychol. 2013;81:846-58.

DOES CHILDHOOD POSITIVE SELF-PERCEPTUAL BIAS MEDIATE ADOLESCENT RISKY BEHAVIOR IN YOUTH FROM THE MTA STUDY.

Hoza B, McQuade JD, Murray-Close D, et al.

Objective: This study's primary aim was to examine whether the positive self-perceptual bias present in many youth with attention-deficit/hyperactivity disorder (ADHD; Hoza et al., 2004; Hoza, Pelham, Dobbs, Owens, & Pillow, 2002) mediates the relation of childhood ADHD status to later risky behaviors.

Method: Using a subset of children with ADHD and comparison children (n=645) from the Multimodal Treatment Study of Children With ADHD, we predicted that a positive bias in childhood would partially or fully mediate the relation between having ADHD and risky driving and sexual behaviors 8 years later.

Results: Results strongly supported this hypothesis for risky driving behavior but only provided limited support for risky sexual behavior.

Conclusions: Taken together, findings suggest that future research should explore whether self-perceptual bias may be a useful target of intervention for children with ADHD.

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J Orthomol Med. 2013;28:101-10.

THE ORTHOMOLECULAR CORRECTION OF METABOLIC IMBALANCES FOUND IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: A RETROSPECTIVE ANALYSIS IN AN OUTPATIENT CLINIC.

Mikirova NA, Casciari JJ, Hunninghake RE.

Background: Attention deficit hyperactivity disorder (ADHD) is characterized by atypically severe inattentiveness, hyperactivity, and impulsiveness. While its cause is unknown, biological and environmental influences are likely.

Objectives: To identify the metabolic imbalances in fatty acid, amino acid, mineral, and pyrrole levels in ADHD patients, and to examine the effectiveness of the nutritional approach in the correction of these imbalances in an outpatient clinic.

Design: Medical records of 116 patients with ADHD treated with nutritional approaches were retrospectively reviewed. Demographics were limited to ensure confidentiality. Blood levels of fatty acids, amino acids, vitamins and minerals, hair analysis of heavy metals and urine pyrrole levels were done on all patients. Comparisons with control (i.e., normal values) were made. Improvements following nutritional interventions were measured and compared to controls.

Setting: The Riordan Clinic (Wichita, KS), an outpatient complementary and alternative medical clinic.

Intervention: Various nutritional interventions (i.e., minerals, vitamins, omega-3 and omega-6 essential fatty acids, flavonoids, probiotics, dietary modifications and chelation of toxic metals by natural substances) were prescribed based on laboratory results.

Main Outcome Measures: Serum fatty acid composition, measurements of minerals (normal and toxic) in hair and, in some cases, in red blood cells (RBC), and assessments of vitamins in serum and pyrroles in urine.

Results: There was a predominance of below-normal docosahexaenoic acid, eicosapentaenoic acid, and gamma-linolenic acid levels; a high incidence of unfavorable arachidonic acid-to-eicosapentaenoic acid and omega-6-to-omega-3 ratios; deficiencies in zinc, magnesium, and selenium levels; and the presence of toxic metals in above-normal amounts.

Conclusions: Our data suggests that at least two of the factors that were the most abnormal, omega-6-to-omega-3 ratios and pyrrole levels, and can in fact improve in subjects undergoing a regimen with nutrient supplementation. While nutritional manipulation did result in improved metabolic profiles in our sample, these results warrant a study of a larger sample, with an attempt to document whether these changes have an effect on improving behavior and cognition in the form of a prospective, controlled clinical study.

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J Paediatr Child Health. 2013.

ASSESSMENT OF CHILDREN WITH LEARNING AND BEHAVIOURAL PROBLEMS: COMPARISON OF A MULTIDISCIPLINARY AND SOLE PAEDIATRICIAN MODEL.

Mittal R, Sciberras E, Sewell J, et al.

Aims: This study aimed to compare multidisciplinary (MD) versus sole paediatrician (SP) assessment models for children with learning and/or behaviour difficulties.

Methods: Children aged 4-12 years referred for an MD or SP assessment of learning and/or behavioural concerns were invited to participate. At baseline, parents completed surveys assessing child behaviour (Strengths and Difficulties Questionnaire; SDQ) and quality of life (QoL) (Pediatric Quality of Life Inventory 4.0; PedsQL). Following the assessment, parents completed a survey evaluating their satisfaction with the assessment. Parents completed a survey at 3-4 months post-assessment assessing: (i) adherence to recommendations; (ii) perceived changes in child functioning; and (iii) child QoL and behaviour.

Results: The parents of 66 children (82% male) participated in the study. Parents reported satisfaction with both assessment models; however, parents in the MD group reported better understanding of their child's

difficulties than the SP group ($P=0.03$). Parents in the MD group were less likely to report that 'recommendations were useful and practical' compared with the SP group ($P=0.01$). There was no significant change in child behaviour or QoL in either group from baseline to 3-4 months post-assessment. **Conclusions:** Parents attending both clinics were satisfied with the assessment process. MD assessment of children with suspected learning and/or behavioural concerns appears to have the additional benefit of helping families to better understand their child's difficulties. Fewer families attending MD clinics reported that recommendations were useful and practical compared with the SP model.

J Psychopathol Behav Assess. 2013;1-11.

EXAMINING ANXIETY AND DEPRESSION AS MODERATORS OF THE ASSOCIATIONS BETWEEN ADHD SYMPTOMS AND ACADEMIC AND SOCIAL PROBLEMS IN HISPANIC ADOLESCENTS.

Becker SP, Fite PJ, Vitulano ML, et al.

The effects of attention-deficit/hyperactivity disorder (ADHD) symptoms on the psychosocial functioning of Hispanic youth have been understudied. It also remains unclear if the well-established associations between ADHD symptoms and academic and social impairment are exacerbated by co-occurring internalizing symptoms. The purposes of the present study were to (1) examine whether ADHD symptoms would be associated with academic and social problems while also controlling for oppositional defiant disorder (ODD) symptoms, and (2) test the hypothesis that anxious and depressive symptoms would moderate the relations between ADHD symptoms and academic and social problems. Participants were 142 at-risk Hispanic adolescents (54 % male, ages 14-19) who reported on their anxious and depressive symptoms, as well as their teachers who reported on adolescents' ADHD symptoms, ODD symptoms, academic problems, and social problems. When the psychopathology variables were included simultaneously in a path model, ADHD was the only domain significantly positively associated with academic problems. In contrast, ODD and depressive symptoms were the only domains significantly positively associated with social problems when all of the psychopathology variables were included in the path model. No moderation effects were found in relation to academic problems, although a significant ADHD null depression interaction was found in relation to social problems. Specifically, ADHD symptoms were not associated with social problems among adolescents who reported low levels of depressive symptoms, but the association between ADHD symptoms and social problems was significant at higher levels of depression. In addition to targeting oppositionality, attending to the combined presence of ADHD and depressive symptoms will be important for reducing the social impairments among Hispanic adolescents.

J Res Med Sci. 2013;18:653-58.

DOES OMEGA-3 SUPPLEMENT ENHANCE THE THERAPEUTIC RESULTS OF METHYLPHENIDATE IN ATTENTION DEFICIT HYPERACTIVITY DISORDER PATIENTS?

Behdani F, Hebrani P, Naseraee A, et al.

Background: Although most of the ADHD (Attention Deficit Hyperactivity Disorder) patients respond to stimulant drugs very well, alternative drugs are required for non responders. It has been revealed that subgroups of patients with ADHD have omega-3 fatty acid deficiency. So, the present study was planned to illustrate the effect of omega-3 supplementation, as an add-on to methylphenidate, on ADHD patients.

Materials and Methods: In this double-blind RCT, ADHD children without any co morbidity, who had been diagnosed by a child and adolescent psychiatrist in child and adolescent university clinic, participated and were randomly divided into 2 groups. The experimental group methylphenidate plus omega-3 capsule (2000mg/d), while control group took methylphenidate plus placebo. Severity of ADHD symptoms were assessed by ADHD rating scale at the baseline and after 2, 4 and 8 weeks of treatment.

Results: 69 patients (experimental = 36, control = 33) aged 7 to 15 participated. A significant reduction of both parent's and teacher's ADHD rating scale scores in both groups was observed. But it couldn't show any difference between two groups. Difference score of parent's at baseline was $1.86 \pm (5/40)$, $P=0.262$,

after 2 weeks $-.70\pm$ (4/30), P_v 0.668, 4 weeks. $19\pm$ (5/60), P_v 0.902 and 8 weeks. $30\pm$ (4/42), P_v 0.845. Difference score of Teacher's at baseline was $-1.56\pm$ (3/45), P_v 0.541, after 2 weeks $-.46\pm$ (6/24), P_v 0.888, 4 weeks. $45\pm$ (5/41), 0.868 and 8 weeks. $73\pm$ (4/18), P_v 0.748.

Conclusion: Omega-3 did not enhance the therapeutic results of methylphenidate in ADHD patients.

J Neurol Sci. 2013;333:e626.

BRAIN LATERALIZATION OF ERP N400 IN CHILDREN WITH ADHD AND THEIR SIBS AND FIRST COUSINS .

Castro-Sierra E, Barragan-Perez E, Flores-Valadez L, et al.

Xia et al. (Psych Res: Neuroimaging 2012; 204:161-167) have noticed regional hypotrophy in ventral anterior, medial dorsal and pulvinar nuclei of left thalamus of children with Attention Deficit/Hyperactivity Disorder. Efferents of pulvinar complex terminate in cortical regions in prefrontal, parietal, occipital, and temporal lobes, and in limbic regions, including the hippocampus. The pulvinar-cortical and pulvinar-limbic connections subserve arousal, attention, learning and memory functions and orientation to visual and auditory stimuli. Thus, structural abnormalities associated with the pulvinar complex in children with ADHD could contribute to disrupted attention. Taking into consideration the genetic components of this disorder, linguistic semantic abilities were studied analyzing ERP > 400 activity of 10 patients with ADHD (7M/3F; avg. age, 10.85; avg. IQ, 99) and 11 of their sibs or first cousins without overt signs of the disorder (5M/6F; avg. age, 11.12; avg. IQ, 96) using high-density EEG (256 channels, EGI, Eugene, OR, USA). Pairs of words with either semantic relatedness (automobile vs. ambulance) or lack of it (automobile vs. animal) appeared on a computer monitor and subjects had to respond on a keyboard whether the words were related or not, while their cortical activity was being measured. Results evidenced diminished > 400 activity in left-hemisphere regions corresponding to anterior cingulum ($p=0.029$), pars opercularis ($p=0.001$), pars triangularis ($p=0.000$) and supramarginal/angular areas ($p=0.000$) in patients, and to anterior cingulum ($p=0.021$), pars opercularis ($p=0.046$) and pars triangularis ($p=0.039$) in their sibs and first cousins.

J Neurol Sci. 2013;333:e693-e694.

DIFFUSION TENSOR IMAGING OF THE CEREBELLUM-PREFRONTAL AREA IN ADHD.

Barragan E, Pilar D, Silvia H, et al.

Objectives: DTI studies have revealed developmental changes in cortical WM pathways in prefrontal regions and in pathways surrounding the basal ganglia and cerebellum in patients with ADHD, which presumably reflect decreasing myelination of axons. It is believed that these changes cause a decrease in the speed of neuronal communication. We hypothesized the presence of abnormal diffusivity in right prefrontal cortex and cerebellum brain regions assessed in vivo using diffusion tensor MRI.

Methods: Twenty three children (ages 7-12 yrs, 11 ADHD patients, 12 controls) were examined as follows: all subjects were scanned while in the supine position with thighs relaxed and parallel to the magnet magnetic field direction. Images were acquired on a 1.5 T imager Diffusion weighted gradients were applied along 15 noncollinear directions with a b -value=800 s/mm². High-resolution images were acquired using 3DT1. Segmentation of the cerebellum CB was manually drawn on midline sagittal 3D-T1 images.

Results: Shows tract distribution in ADHD and healthy controls. We present preliminary results of white matter connectivity of tracts connected cerebellum-prefrontal area. There were no discernible ADHD-Control changes in ADC values along the connected white matter (Fig. 2) while generalized fractional anisotropy is increased ($p=0.08$), as it was reported in recent literature [1]. Length of tracts vs ADC is shown in Fig. 3. In summary, as the study progresses, MD, I1, I2, and I3 will be used in order to further examine frontalcerebellum tracts in patients with ADHD.

J Neurol Sci. 2013;333:e592.

ASSOCIATION BETWEEN DBH GENE POLYMORPHISMS AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN KOREAN CHILDREN.

Lim MH, Lee CM, Kwon HJ.

Attention deficit hyperactivity disorder (ADHD) is a common disorder of the school-age population. ADHD is familial and genetic studies estimate heritability at 80-90%. The aim of the present study was to investigate the association between the genetic type and alleles for DBH gene in Korean children with ADHD. The sample consisted of 142 ADHD children and 139 control children. We diagnosed ADHD according to DSM-IV. ADHD symptoms were evaluated with Conners' Parent Rating Scales and Dupaul Parent ADHD Rating Scales. Blood samples were taken from the 281 subjects, DNA was extracted from blood lymphocytes, and PCR was performed for DBH polymorphism. Alleles and genotype frequencies were compared using the Chi-square test. We compared the allele and genotype frequencies of DBH gene polymorphism in the ADHD and control groups. This study showed that there was a significant correlation among the frequencies of the rs1611115 (OR=0.64, 95% CI=0.42-0.97, p=0.034) of alleles of DBH, but the final conclusions are not definite. Follow-up studies with larger patient or pure subgroups are expected. These results suggested that DBH might be related to ADHD symptoms.

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J Neurol Sci. 2013;333:e585.

THE EFFECT OF EPILEPSY COMORBIDITY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Sim GY, Kim WS.

Purpose: The rate of attention deficit hyperactivity disorder (ADHD) is higher in children with epilepsy than in the general population. The 31-40% of ADHD is accompanied with epilepsy. There are not many studies in ADHD with epilepsy. So we checked the effect of epilepsy comorbidity in children with ADHD.

Methods: This study retrospectively examined the effect of epilepsy comorbidity in children with ADHD. We studied 34 ADHD children with epilepsy at Chungbuk National University Hospital and 38 ADHD children without epilepsy at Cheonju St. Mary's Hospital because of ADHD with epilepsy or ADHD from January 2005 to June 2010.

Result: In ADHD with epilepsy, there were 12 cases (35.2%) of partial seizure, 11 cases (32.2%) of generalized seizure, 11 other cases (32.2%). Among the abnormal sites found in EEG there were 15 cases in the frontal lobe, 7 cases in the central lobe, 6 cases in the temporal lobe, and 3 cases in the occipital lobe. In ADHD with epilepsy, the combined type is 76.4% and in ADHD without epilepsy, the inattentive type is 50.5% (P=0.004). There is more learning disability in ADHD with epilepsy than in ADHD without epilepsy (P=0.01).

Conclusion: In ADHD with epilepsy, the combined type showed 76.4%. There is more learning disability in ADHD with epilepsy than in ADHD without epilepsy. This study showed the effect of epilepsy comorbidity in children with ADHD.

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J Neurol Sci. 2013;333:e582.

NEUROPSYCHOLOGICAL DEFICITS IN ADHD: DEVELOPMENT OF A CLASSIFICATION SYSTEM.

Gupta R.

Background: Recent experimental literature on ADHD has identified unique underlying cognitive dysfunction, specific to ADHD. Therefore, there is a need to incorporate information on cognitive mechanisms underlying ADHD and inculcate such information in the diagnostic system, which would provide a more sensitive as well as specific tool in differential diagnosis of ADHD.

Objective: The present study evaluated the diagnostic capabilities of certain measures based on cognitive-motivational tests that were chosen with respect to the specific cognitive deficits in Attention Deficit Hyperactivity Disorder (ADHD).

Methods: A total of 240 children (120 with ADHD and 120 healthy controls) in the age range of 6-9 years and 32 children with Oppositional Defiant Disorder (ODD) (aged 9 years) participated in the study. Stop-

signal, attentional-disengagement, attentional-network, and choice-delay test were administered to all the participants. A total of nineteen parameters were derived from the four tests. Receiver operating characteristic (ROC) analysis and multinomial logistic regression (MLR) was performed to examine the diagnostic efficiency of each parameter.

Results: MLR was performed for combining parameters across tests. Data fusion produced improved overall diagnostic accuracy and a combination of stop-signal reaction time, post-error-slowness, mean delay, switch costs, and %LDR produced overall classification accuracy of 97.8% and with internal validation, the overall accuracy was 92.2%.

Conclusions: Combining performance from different tests enabled an accurate classification of ADHD children from healthy controls and those with ODD. The study has theoretical and clinical implications for the theories of executive control mechanisms that underlie the pathology of ADHD.

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J Neurol Sci. 2013;333:e694.

RESTING STATE IN LATIN AMERICAN CHILD WITH ADHD.

Barragan E, Silvia H, Pilar D, et al.

Objectives: ADHD is a neurological disorder in children. This illness is considered to be 80% originated by genetic factors. Here we compared infant Latin ADHD patients with healthy ones. We discuss the differences with previous studies that used different genetic pools.

Methods: 30 volunteers (8.4 (plus or minus) 2 years, both sexes) were divided in two groups, healthy (H) and ADHA (AD). Volunteers laid in an MR scanner in silence while 150 brain volumes covering the whole of the brain were acquired. Resting state analysis was performed using DPARSF software. Low frequencies under 0.08 Hz were kept.

Results: Figure 1A and 1B present the results of a comparison between H and AD patients (H > AD in green and AD > H in red). H subjects presented strong left lateralization (80% vs. 20% structures). AD patients presented a stronger right lateralization (55% vs. 45%).

Conclusions: AD patients had a larger predominance of right hemisphere activations over left in contrast to healthy subjects. Previous work has reported strong involvement of the brain stem and the anterior cingulate gyrus for AD patients compared to H which we did not find. Never reported correlations with the frontal gyrus and the posterior cingulate cortex were found. Considering that similar analysis methods were followed as in previous studies, we believe that the differences shown arise by the different genetic origin of volunteers.

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Neuropsychiatr Dis Treat. 2013;9:1457-61.

PERSISTING PRIMITIVE REFLEXES IN MEDICATION-NAIVE GIRLS WITH ATTENTION-DEFICIT AND HYPERACTIVITY DISORDER.

Konicarova J, Bob P, Raboch J.

Background and objectives: Recent and historical findings suggest that later-developed functions during brain ontogenesis related to higher levels of cognitive and motor integration tend to replace the older, more primitive, ones, and the persistence of the older functions may be linked to specific neuropsychiatric disorders. Currently, there is growing evidence to suggest that persisting primitive reflexes may be related to developmental and neurodegenerative disorders. Preliminary data also suggest that persisting primitive reflexes may be specifically linked to attention-deficit and hyperactivity disorder (ADHD).

Methods: In the study reported here, we tested to what extent the persisting primitive asymmetric tonic neck reflex and symmetric tonic neck reflex are related to ADHD symptoms measured by Conners' Parent Questionnaire in 35 medication-naive girls of school age (8-11 years) with ADHD. The results were compared with those of a control group of 30 girls of the same age.

Results: This study showed that persisting primitive reflexes are closely linked to ADHD symptoms.

Conclusion: The data suggest that ADHD symptoms may be linked to more primitive neural mechanisms interfering with higher brain functions due to insufficiently developed cognitive and motor integration.

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Neuropsychology. 2013;27:537-45.

SEPARATE COMPONENTS OF EMOTIONAL GO/NO-GO PERFORMANCE RELATE TO AUTISM VERSUS ATTENTION SYMPTOMS IN CHILDREN WITH AUTISM.

Yerys BE, Kenworthy L, Jankowski KF, et al.

Objective: The present investigation examined whether higher functioning children with autism would demonstrate impaired response inhibition performance in an emotional go/no-go task, and whether severity of attention-deficit/hyperactivity disorder (ADHD) or autism symptoms correlated with performance.

Method: Forty-four children (21 meeting criteria for autism; 23 typically developing controls [TDCs]) completed an emotional go/no-go task in which an emotional facial expression (angry, fearful, happy, or sad) was the go stimulus and a neutral facial expression was the no-go stimulus, and vice versa.

Results: The autism group was faster than the TDC group on all emotional go trials. Moreover, the children in the autism group who had the fastest reaction times on emotional go trials were rated as having the greatest number of symptoms (Autism Diagnostic Observation Schedule Social + Communication score), even after accounting for the association with ADHD symptoms. The autism group also made more impulsive responses (i.e., lower d' , more false alarms) than the TDC group on all trials. As d' decreased or false alarms increased, so did ADHD symptoms. Hyperactivity/impulsivity symptoms were significantly correlated with false alarms, but inattention symptoms were not. There was not a significant relationship between no-go false alarms and autism symptoms; even after partialing out associations with autism symptoms, the significant correlation between ADHD symptoms and no-go false alarms remained.

Conclusion: The present findings support a comorbidity model that argues for shared and independent risk factors, because ADHD and autism symptoms related to independent aspects of emotional go/no-go performance.

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Nord J Psychiatry. 2013;67:351-59.

PATIENT PREFERENCES AND WILLINGNESS-TO-PAY FOR ADHD TREATMENT WITH STIMULANTS USING DISCRETE CHOICE EXPERIMENT (DCE) IN SWEDEN, DENMARK AND NORWAY.

Glenngard AH, Hjelmgren J, Thomsen PH, et al.

Background: The choice between different attention-deficit/hyperactivity disorder (ADHD) medications depends on different drug attributes. Economic evaluations of drugs often disregard the utility of other attributes compare with the drugs' efficacy.

Aims: The aim of this study was to assess patient's preferences and elicit willingness-to-pay (WTP) for different drug attributes in the treatment of ADHD.

Methods: 285 patients (117 parents for children below 15 years, 52 adolescents 15-17 years and 116 adults aged 18 years and above) from Sweden, Denmark and Norway completed a questionnaire concerning their ADHD drug treatment, and answered questions on their preferences using a discrete choice experiment (DCE). Included attributes were effectiveness, side-effects, dosing and price.

Results: Effectiveness was the most important attribute, followed by side-effects and the number of dosings per day (all $P < 0.001$). The estimated monthly WTP for a drug generating full effectiveness, no side-effects and once-daily dosing was (euro)790 for adolescents and (euro)360 for adults. The estimated WTP for ADHD drugs with characteristics similar to existing drugs on the market was higher or in line with market prices ((euro)37-180 for adolescents and (euro)16-80 for adults). Regarding experience with current treatment, 19% of all patients in the study reported good functioning during the morning, day and evening.

Conclusions: The gap between the monetary valuation of existing products and an optimally valued product suggest that there is room for improvements in the clinical management of ADHD. The results suggest that DCE is a method that can be used to value not only hypothetical scenarios but also can be used to value and distinguish between real-life scenarios.

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Noropsikiyatr Ars. 2013;50:244-51.

THE EFFECTIVENESS OF AN INTERPERSONAL COGNITIVE PROBLEM-SOLVING STRATEGY ON BEHAVIOR AND EMOTIONAL PROBLEMS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY.

Ozcan CT, Oflaz F, Turkbay T, et al.

Introduction: This study was designed to evaluate the effectiveness of the "I Can Problem Solve" (ICPS) program on behavioral and emotional problems in children with attention deficit hyperactivity disorder (ADHD).

Methods: The subjects were 33 children with ADHD aged between 6 to 11 years. The study used a pre- and post-test quasi-experimental design with one group. The researchers taught 33 children with ADHD how to apply ICPS over a period of 14 weeks. The Child Behavior Checklist for Ages 6-18 (Teacher Report Form) and the Diagnostic and Statistical Manual of Mental Disorders, 4th edition Text Revision (DSM-IV-TR) Based Disruptive Behavior Disorders Screening and Rating Scale (parents' and teacher's forms) were used to evaluate the efficacy of the program. The scales were applied to parents and teachers of the children before and after the ICPS program.

Results: The findings indicated that the measured pre-training scores for behavioral and emotional problems (attention difficulties, problems, anxious/depressed, withdrawn/depressed, oppositional defiant problems, rule breaking behaviors, and aggressive behaviors) were significantly decreased in all children post-training. In addition, children's total competence scores increased (working, behaving, learning and happy) after the ICPS program.

Conclusion: According to the results, it is likely that, ICPS would be a useful program to decrease certain behavioral and emotional problems associated with ADHD and to increase the competence level in children with ADHD. An additional benefit of the program might be to empower children to deal with problems associated with ADHD such as attention difficulties, hyperactivity-impulsivity, and oppositional defiant problems.

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Patient Preference Adherence. 2013;7:987-95.

PREDICTORS AND CONSEQUENCES OF ADHERENCE TO THE TREATMENT OF PEDIATRIC PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CENTRAL EUROPE AND EAST ASIA.

Hong J, Novick D, Treuer T, et al.

Purpose: To assess baseline predictors and consequences of medication non-adherence in the treatment of pediatric patients with attention-deficit/hyperactivity disorder (ADHD) from Central Europe and East Asia.

Patients and methods: Data for this post-hoc analysis were taken from a 1-year prospective, observational study that included a total of 1,068 newly-diagnosed pediatric patients with ADHD symptoms from Central Europe and East Asia. Medication adherence during the week prior to each visit was assessed by treating physicians using a 5-point Likert scale, and then dichotomized into either adherent or non-adherent. Clinical severity was measured by the Clinical Global Impressions-ADHD-Severity (CGI-ADHD) scale and the Child Symptom Inventory-4 (CSI-4) Checklist. Health-Related Quality of Life (HRQoL) was measured using the Child Health and Illness Profile-Child Edition (CHIP-CE). Regression analyses were used to assess baseline predictors of overall adherence during follow-up, and the impact of time-varying adherence on subsequent outcomes: response (defined as a decrease of at least 1 point in CGI), changes in CGI-ADHD, CSI-4, and the five dimensions of CHIP-CE.

Results: Of the 860 patients analyzed, 64.5% (71.6% in Central Europe and 55.5% in East Asia) were rated as adherent and 35.5% as non-adherent during follow-up. Being from East Asia was found to be a strong predictor of non-adherence. In East Asia, a family history of ADHD and parental emotional distress

were associated with non-adherence, while having no other children living at home was associated with non-adherence in Central Europe as well as in the overall sample. Non-adherence was associated with poorer response and less improvement on CGI-ADHD and CSI-4, but not on CHIP-CE.

Conclusion: Non-adherence to medication is common in the treatment of ADHD, particularly in East Asia. Non-adherence was associated with poorer response and less improvement in clinical severity. A limitation of this study is that medication adherence was assessed by the treating clinician using a single item question.

Pediatr Neurol. 2013.

SOCIAL BEHAVIOR AND COMORBIDITY IN CHILDREN WITH TICS.

Pringsheim T, Hammer T.

Objectives: To examine the characteristics of children with coexisting tics and autism spectrum disorder and determine if children with tics have deficits in social behavior.

Methods: Descriptive study of children referred for tics over 18 months. Parents completed the Social Responsiveness Scale and the Social Communications Questionnaire; children screening positive on these measures were evaluated for autism spectrum disorder. Characteristics of children who were diagnosed with both disorders are described. Subscale scores on the Social Responsiveness Scale for children with tics without a comorbid autism spectrum disorder were compared. The relationship between a comorbid diagnosis of attention deficit hyperactivity disorder and autism spectrum disorder symptoms was explored using logistic and linear regression.

Results: One hundred and fourteen children were evaluated. Children with a tic disorder and autism spectrum disorder had significantly higher rates of comorbid attention deficit hyperactivity disorder ($P = 0.005$), rage attacks ($P = 0.006$), and oppositional defiant disorder ($P = 0.007$) than children without autism spectrum disorder. Mean tic severity and treatment rates did not differ between groups. Mean subscale scores on the Social Responsiveness Scale for children without autism spectrum disorders fell into the clinically significant range for autistic mannerisms only. All Social Responsiveness Scale scores were significantly increased by an attention deficit hyperactivity disorder diagnosis ($P < 0.0001$).

Conclusion: Children referred for assessment of tics should be screened for autism spectrum disorders. There is a subgroup of children with multiple neuropsychiatric comorbidities who suffer from social dysfunction and autistic mannerisms outside of an autism spectrum disorder diagnosis.

Pharmacogenomics J. 2013;13:476-80.

ASSOCIATION OF A CARBOXYLESTERASE 1 POLYMORPHISM WITH APPETITE REDUCTION IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER TREATED WITH METHYLPHENIDATE.

Bruxel EM, Salatino-Oliveira A, Genro JP, et al.

Carboxylesterase 1 is the enzyme involved in methylphenidate (MPH) metabolism. The aim of this study was to evaluate the association between a -75 T>G polymorphism and appetite reduction in children with attention-deficit/ hyperactivity disorder (ADHD). A sample of 213 children with ADHD was investigated. The primary outcome was appetite reduction measured by the Barkley Stimulant Side Effect Rating Scale applied at baseline, at 1 and 3 months of treatment. MPH doses were augmented until no further clinical improvement or significant adverse events occurred. The G allele presented a trend for association with appetite reduction scores ($P=0.05$). A significant interaction between the G allele and treatment over time for appetite reduction scores was also observed ($P=0.03$). The G allele carriers presented a higher risk for appetite reduction worsening when compared with T allele homozygotes (odds ratio=3.47, $P=0.01$). The present results suggest an influence of carboxylesterase 1 -75 T>G polymorphism on the worsening of appetite reduction with MPH treatment in youths with ADHD.

PLoS ONE. 2013;8.

ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER AND VIOLENCE IN THE POPULATION OF ENGLAND: DOES COMORBIDITY MATTER?

Gonzalez RA, Kallis C, Coid JW.

Background: It is unclear whether the association between Attention Deficit/Hyperactivity Disorder (ADHD) and violence is explained by ADHD symptoms or co-existing psychopathology. We investigated associations of ADHD and its symptom domains of hyperactivity and inattention, among individuals reporting violence in the UK population.

Methods: We report data from the Adult Psychiatric Morbidity Survey (2007), a representative sample of the household population of England. A randomly selected sample of 7,369 completed the Adult Self-Report Scale for ADHD and the self-reported violence module, including repetition, injury, minor violence, victims and location of incidents. All models were weighted to account for non-response and carefully adjusted for demography and clinical predictors of violence: antisocial personality, substance misuse and anxiety disorders.

Results: ADHD was moderately associated with violence after adjustments (OR 1.75, $p=.01$). Hyperactivity, but not inattention was associated with several indicators of violence in the domestic context (OR 1.16, $p=.03$). Mild and moderate ADHD symptoms were significantly associated with violence repetition, but not severe ADHD where the association was explained by co-existing disorders. Stratified analyses further indicated that most violence reports are associated with co-occurring psychopathology.

Conclusions: The direct effect of ADHD on violence is only moderate at the population level, driven by hyperactivity, and involving intimate partners and close persons. Because violence associated with severe ADHD is explained by co-existing psychopathology, interventions should primarily target co-existing disorders.

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PLoS ONE. 2013;8.

FEW EFFECTS OF FAR TRANSFER OF WORKING MEMORY TRAINING IN ADHD: A RANDOMIZED CONTROLLED TRIAL.

Egeland J, Aarlien AK, Saunes BK.

Objective: Studies have shown that children with ADHD profit from working memory training, although few studies have investigated transfer effects comprehensively. The current Randomized Controlled Trial analyzes transfer to other neuropsychological (NP) domains, academic performance and everyday functioning at home and school.

Method: Sixty-seven children with ADHD were randomized into a control group or a training group. The training group underwent Cogmed's RoboMemo program. All participants were assessed pre-training, immediately after and eight months later with a battery of NP tests, measures of mathematical and reading skills, as well as rating scales filled out by parents and teachers.

Results: There was a significant training effect in psychomotor speed, but not to any other NP measures. Reading and mathematics were improved. There were no training induced changes in symptom rating scales either at home or at school. The increased reading scores remained significant eight months later.

Conclusion: The study is the most comprehensive study of transfer effects to date, and with mixed results compared to previous research. More research is needed regarding how to improve the training program and the conditions and thresholds for successful training.

Trial Registration: Controlled-Trials.com ISRCTN19133620.

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PLoS ONE. 2013;8.

ON THE TEMPORAL CHARACTERISTICS OF PERFORMANCE VARIABILITY IN ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Feige B, Biscaldi M, Saville CWN, et al.

Increased intra-subject variability of reaction times (ISV-RT) is one of the most consistent findings in attention-deficit/hyperactivity disorder (ADHD). Although the nature of this phenomenon is still unclear, it has been hypothesised to reflect interference from the Default Mode Network (DMN). So far, ISV-RT has been operationally defined either as a frequency spectrum of the underlying RT time series, or as a measure of dispersion of the RT scores distribution. Here, we use a novel RT analysis framework to link these hitherto unconnected facets of ISV-RT by determining the sensitivity of different measures of RT dispersion to the frequency content of the underlying RT time series. N=27 patients with ADHD and N=26 healthy controls performed several visual N-back tasks. Different measures of RT dispersion were repeatedly modelled after individual frequency bands of the underlying RT time series had been either extracted or suppressed using frequency-domain filtering. We found that the intra-subject standard deviation of RT preserves the "1/f noise" characteristic typical of human RT data. Furthermore and most importantly, we found that the ex-Gaussian parameter (τ) is rather exclusively sensitive to frequencies below 0.025 Hz in the underlying RT time series and that the particularly slow RTs, which nourish (τ), occur regularly as part of an quasi-periodic, ultra-slow RT fluctuation. Overall, our results are compatible with the idea that ISV-RT is modulated by an endogenous, slowly fluctuating process that may reflect DMN interference.

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Psychiatr Invest. 2013;10:253-58.

NOCTURNAL ENURESIS IS ASSOCIATED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND CONDUCT PROBLEMS.

Park S, Kim BN, Kim JW, et al.

Objective There are no published prevalence estimates of elimination disorders and their association with disruptive-behavior disorders among children in the Asian region using standardized diagnostic interviews. This study was conducted to determine the prevalence of elimination disorders and its association with disruptive-behavior disorders in a representative sample of children in Seoul, Korea.

Methods The diagnosis of enuresis and encopresis was derived from parent-reported data for "enuresis and encopresis," collected using the Diagnostic Interview Schedule for Children, from a representative sample of 6- to 12-year-old children (n=1,645) who participated in the 2005 Seoul Child and Adolescent Mental Health Survey. Prevalence data for attention deficit and disruptive-behavior disorders were collected from the same sample.

Results The overall 12-month prevalence of nocturnal enuresis and encopresis was 1.8% and 0.6%, respectively. Enuresis and encopresis prevalence in boys was significantly greater than that in girls. Enuresis and encopresis was most common at 7 to 9 years of age. Enuresis was significantly associated with ADHD (OR 2.6, 95% CI 1.0-6.9) and conduct disorder (CD; OR 4.7, 95% CI 1.0-22.4).

Conclusion Enuresis is significantly associated with ADHD and CD, so these conditions must be assessed together during the evaluation of children with enuresis.

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Psychiatry Res. 2013;209:740-41.

EFFECTS OF STIMULANTS AND ATOMOXETINE ON CORTISOL LEVELS IN CHILDREN WITH ADHD.

Isaksson J, Hogmark A, Nilsson KW, et al.

Children with attention deficit hyperactivity disorder (ADHD) have lower diurnal cortisol levels than non-ADHD comparison subjects. Aiming at elucidating the effects of medications used to treat ADHD, we investigated saliva cortisol in children with ADHD: 20 without medication, 147 on methylphenidate, and 21 on atomoxetine. The only significant finding was that children on atomoxetine had higher cortisol levels at bedtime than unmedicated children.

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Psychoneuroendocrinology. 2013;38:2327-36.

HPA AXIS REACTIVITY IN EARLY CHILDHOOD: ASSOCIATIONS WITH SYMPTOMS AND MODERATION BY SEX.

Kryski KR, Smith HJ, Sheikh HI, et al.

Sex differences in rates of internalizing disorders have been attributed in part to heightened sensitivity to stress in females. While the sex difference in disorder rates becomes most pronounced in adolescence, developmental research suggests that stress reactivity in girls may be related to elevated internalizing symptoms even in childhood. We therefore examined whether child sex moderated associations between symptoms of psychopathology and cortisol reactivity to a standardized stress task in 409 three-year-old community-dwelling children. Anxious symptoms were associated with elevated cortisol reactivity, but only in girls. Externalizing symptoms were unrelated to baseline cortisol or cortisol reactivity, and no evidence for moderation by child sex was found. Results suggest that cortisol reactivity to stress in early childhood has a sex-specific association with girls' internalizing symptoms.

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CORRESPONDENCE

More and better should be done to guarantee evidence-based management of ADHD in children across Europe

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Dear Editor,

In their July issue paper, Hodgkins et al. concluded that “European patients may benefit from better standardization of ADHD management across countries and additional treatment options” [2].

According to science and human rights, all management should be appropriate, evidence-based, and up-to-date, and all patients should be guaranteed the best available treatment. Thus, “better standardization” and “additional treatment options” refer to a limited retrospective study that was also potentially dated.

The broad, discretionary criteria in sampling both physicians and patients consistently affected results, leading to imbalance within and between countries. For example, despite the study's selection of “physicians with ADHD expertise,” 15 % of patients in the Netherlands and 24 % in UK received a diagnosis of ADHD without either of the two main diagnostic criteria (ICD-10 or DSM-IV).

Starting therapy, duration, and intensity/dosage were not reported. The authors' comments concerning therapy switch, satisfaction, outcome, and treatment management are thus not supported by adequate analyses. Authors reported, for example, that symptom control was strongest in patients receiving long-acting methylphenidate (36 %) and weakest in patients receiving behavioral therapy (BT) (only 16 %), but duration and intensity should be considered in BT.

Another important bias of the study is the long follow-up period (2–5 years), knowing that ADHD symptoms are affected by the duration and type of treatment [3].

Since only 34.5 % of included patients were treated with a combination of pharmacotherapy and BT, according to NICE guideline recommendations [4], only 30.8 % of patients would be expected to show “complete symptom control.”

Lastly, the profile of ADHD management resulting from this study is completely different from the Italian reality [1, 5].

One of the acknowledged needs of ADHD patients is effective evidence-based interventions, and this can be achieved through (useful) data collection, assessment of prevalence, case identification, and outcome measurements. This work does not seem to contribute to this aim.


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EDITORIALS

Prescribing methylphenidate for moderate ADHD

Has NICE guidance unwittingly exposed a new challenge for assessing this condition?

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Why has the National Institute for Health and Care Excellence (NICE) issued a reminder that first line treatment for moderate attention-deficit/hyperactivity disorder (ADHD), which affects about 8% of school aged children and young people in the United Kingdom,¹ should not include methylphenidate?² This recent bulletin follows the annual report by the Care Quality Commission, which showed that methylphenidate prescriptions for ADHD in primary care in England rose by 56% between 2007 and 2013.³

The 2006 NICE technology appraisal guidance for the use of methylphenidate in ADHD in children stated that “it is not anticipated that this guidance will result in a major increase over current trends in the rate of prescribing for ADHD.”⁴ Although the Care Quality Commission report didn’t clarify what proportion of methylphenidate prescriptions are for moderate ADHD, NICE’s bulletin suggests that the institute is worried that it has underestimated prescription trends and that clinicians may not be heeding its guidance. What could be causing this increase in methylphenidate use?

The commission’s report explains that between 2011 and 2012 the prescription of methylphenidate in primary care continued to rise steadily, by 11%. In the commission’s opinion “this reflects increased diagnosis of, and prescribing for” the treatment of ADHD.³ However, the NICE guideline on ADHD for children and adults,⁵ and its recently published quality standard,¹ do not recommend drugs as first line treatment for school aged children and young people with moderate ADHD, or for any preschool children. It does recommend drugs as first line treatment for “severe” ADHD, which NICE estimates has a prevalence of 1%.⁴ NICE advises offering children and young people with moderate ADHD referral to a psychological group treatment programme.¹ It defines “moderate ADHD” as when “symptoms of hyperactivity/impulsivity and/or attention, or all three, occur together and are associated with at least moderate impairment in multiple settings and multiple domains.”⁵

The adjective “moderate” isn’t clarified, but the *Oxford English Dictionary* defines it as “average in amount, intensity, quality or degree.” So, moderate means average, but what does average mean in the context of behaviour in school aged children? NICE guidance on ADHD infers confident clinical discrimination

between moderate and severe, but is there a valid and reliable severity rating process in the assessment of ADHD?

Neurodevelopmental conditions are conceptualised as disorders of behaviour that can be assessed by direct observation.⁶ Two decades of successful research innovation have enabled the assessment of autism spectrum disorder to become the paradigm for this observational approach. In autism, instruments are increasingly used for taking the history of parents and carers and direct clinical assessment of the patient. When assessing patients, experienced clinicians using the *Autism Diagnostic Observation Schedule* can grade the severity of clinical presentation according to coding outcomes.⁷ ADHD researchers have developed instruments to help gather information from parents, carers, and teachers that contain a severity measure, in terms of the degree rated by the clinician, or the level of score provided by the informing adult (for example, the ADHD rating scale⁸). However, ADHD assessment research has not provided an equivalent of the schedule for assessing autism. In the clinic (or classroom/playground) it is not easy to judge accurately whether the child has moderate or severe ADHD, because the assessing clinician relies mostly on information provided by non-clinicians.⁶

An additional factor that may contribute to the Care Quality Commission’s findings is that the diagnosis of ADHD is inextricably linked with consequent drug treatment for its core symptoms, whereas this is not the case in autism.⁹ Doctors may also not have access to psychological therapy for the large numbers of patients with moderate ADHD, even if they request it. For all of these reasons, the current increasing tendency for doctors to prescribe methylphenidate for any diagnosis of ADHD is unsurprising. Because of this growing trend, precious capacity within child and adolescent psychiatry (and, to a lesser extent, community paediatrics) has become monopolised by demands for ADHD drugs.³ We need to consider other issues as well.

Why hasn’t research into the assessment of ADHD been able to deliver an equivalent of the schedule for assessing autism? Can we really go on diagnosing up to 9% of our children with a psychiatric condition that cannot be directly assessed in a valid and reliable way? The prescription of methylphenidate for ADHD often spans most of a patient’s childhood and adolescence, if not beyond. How effective are busy clinicians

at identifying those patients who were initially judged to have severe ADHD but who now have moderate disease and no longer need drug treatment?

The NICE bulletin quotes Professor Tim Kendall, consultant psychiatrist and member of the ADHD guideline's development group, speaking to BBC Radio 4's *Today* programme about the commission's report.² When asked about the side effects of methylphenidate, he said that, if taken for a year it is likely to reduce children's growth by about three quarters of an inch. He also said that there was increasing evidence that the use of methylphenidate "precipitates self harming behaviour in children," and that there was no evidence that the drug reduces the long term problems associated with ADHD. Given the burgeoning cost of rising numbers of methylphenidate prescriptions, alongside often irreversible iatrogenic consequences (such as growth retardation), is there really no other way to help these children and their families?

Competing interests: I have read and understood the BMJ Group policy on declaration of interests and declare the following interests: I am an *Autism Diagnostic Observation Schedule (ADOS)* trainer and have been paid for co-leading a training course; I have been paid by the Scottish government to co-lead research into autism assessment in Scotland; I

am chair of the review of the SIGN guideline on autism spectrum disorders.

Provenance and peer review: Commissioned; not externally peer reviewed.

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Re: Prescribing methylphenidate for moderate ADHD

Martel Martel, Consultant Paediatrician

Southeastern Health and Social Care Trust, Dundonald, Northern Ireland

19 October 2013

Dear Editor

I am appalled that the BMJ commissioned an editorial on medication for the treatment of ADHD from a psychiatrist who obviously spends little time working in the area. It is clear to me that the editor of the journal has an anti-medication agenda which was being promoted. At the very least there should have been the opportunity for a side-by-side rebuttal.

The article misrepresents NICE guideline which list a number of situations in which it is appropriate to offer medication to moderate ADHD patients, especially when behaviour therapy fails, which it usually does. It ignores the fact that NICE states that Dexamphetamine is licensed for the treatment of ADHD in child 3 years of age and older. (This is not what the BNF says but that is in fact the license indication for treatment.)

The worst sin, however, is the final paragraph in which the NICE bulletin is quoted as a reference for the unsupported comments of Professor Tim Smith. The bulletin itself is an awful piece of work from an organisation that is supposed to rely on evidence based medicine. Medication for ADHD has been shown to reduce self-harm, to lower the incidence of antisocial behaviour and drug misuse and to improve driving skills thus lowering the chance of an accident. That is what the data shows. None of what Professor Smith is quoted as saying is backed by the most recent evidence.

Severe ADHD is easy to spot. The child has already been excluded from school, perhaps in P1. The arguments about what constitutes moderate ADHD will persist but should we deny treatment to a student who struggles to do C level work because of their moderate ADHD symptoms when their IQ suggests they have the potential for A's? Substantial clinical improvement in behaviour and academic productivity is regularly seen in our clinic. In the longterm what is the effect of persistent failure on that child's self esteem if he is denied medication?

Methylphenidate is classified as a pypiridine. This class of drugs includes bronchodilators which are also "stumulents". We know that mild to moderate allergic asthma can be treated with aggressive environmental control to good effect. We do not, however, insist that the child be forced to live in an environmental bubble for three months before we offer a bronchodilator, let alone inhaled steroids, in order to relieve the symptoms.

Dr McClure's area of expertise is Autism. Perhaps he should instead have addressed the massive increase in the use of Risperidone in that group of patients over the past five years rather than commenting on the treatment of a condition of which he seems to have little understanding of the science or compassion for the patients.

Competing interests: I am a consultant working in the area of ADHD and Autism. I have participated in drug trials for ADHD and I am on the speaker panel for several Pharma companies.

Re: Prescribing methylphenidate for moderate ADHD

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21 October 2013

Dr McClure is right to point out that NICE have got themselves in a bit of a mess with this one. As a member of the expert working group and then the lead reviewer for the NICE ADHD guideline, it became clear to me that evidence counted little compared to the opinions of the guideline group members. This was particularly so on the question of the validity of the diagnosis (where, by their own criteria, the group found little to support the validity of the ADHD construct) and the question of medication use. NICE's single most important recommendation was for medication to be used as a first line treatment in "severe" attention deficit hyperactivity disorder (ADHD)[1].

However, Like other systematic reviews of ADHD medication treatment, NICE noted the inadequate reporting of study methodology, possible bias, limited reliability of results, and inadequate data regarding adverse events, correctly concluding that the evidence does not support using medication as a first line treatment for mild or moderate ADHD. Yet NICE concluded that medication should be used as a first line treatment in "severe" ADHD, with only one reference cited in support of this [2], which concludes that in a well known large American trial, the more severe subgroup showed a larger decrease in symptoms with a trial. However, this data was gathered at 14 months after the beginning of the study; Swanson et al analyzing the same group of patients after 36 months could not find support for beneficial long term effects of medication over behaviour therapy, even in those with more severe symptoms [3]. Other naturalistic studies have come to similar conclusions that medication offers much prospect of beneficial long term outcomes.

Thus there is little evidence that the benefits outweigh the harms in the long term use of stimulants for ADHD of any severity. As NICE left several non-evidence based 'get out clauses' for medication use, it was predictable that the trend for escalating stimulant use that they are now concerned about would continue uninterrupted.

Where I think Dr McClure's arguments are unconvincing is his turning to the methodologies used in Autism diagnosis as a route to developing ways of distinguishing between severe and moderate presentations. The issue of finding a rational basis for arriving at cut-off's between moderate and severe, however, will never be solved in this way, as they haven't been solved in autism. Having more criteria doesn't remove the subjectivity inherent in how Autism or ADHD are conceptualised. The expansion in the numbers deemed Autistic has been even more astonishing and just as concerning as the expansion in the numbers deemed to have ADHD. Neither condition has any 'hard' objective data by which one can support the diagnosis and thus both rely on ideologically driven ideas about categorical classifications (such as mild, moderate, and severe) of heterogeneous presentations. I'm afraid for this one it's back to the drawing board, unless we find reliable ways of uncovering endo-phenotypic markers (something which seems to me increasingly unlikely for either autism or ADHD).

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Competing interests: None declared

Re: Prescribing methylphenidate for moderate ADHD

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4 November 2013

Although focused on the UK situation, McClure's editorial refers to further considerations, both general and specific for ADHD management.

Drug prescription trends are affected by different variables that change over time.[1] A systematic and continuous monitoring by health institutions can contribute to planning early interventions to rectify problems and guarantee the most appropriate, available treatment. Appraisal guidelines (such as the NICE documents) can lead to a more rational use of drugs, but monitoring their impact in practice is mandatory, as well as measuring their reliability and sustainability.[2]

In the child and adult psychiatric areas psychological treatment alone, or in association with drug therapy, should be guaranteed to all patients (and their families) as part of a multimodal approach. Unfortunately, the available health system resources and management limit the implementation of such a recognized priority worldwide.[3] Drug prescription alone may often result as easier, cheaper, and as the only available option, even though it is often effective for limited time. In such a context, the categorical or dimensional types of classifications (such as mild, moderate, and severe) are more academic attitudes than useful approaches in/for the practice.

Concerning ADHD management, an official, national registry was activated in Italy in September 2007 in an attempt to limit these problems.[4] Patients for whom methylphenidate and atomoxetine (the only two drugs with a specific indication for ADHD that are available in Italy) are prescribed require a strict diagnostic assessment of the disorder prior to treatment, and systematic monitoring during treatment. Local reference centres send patient information to the national registry. Data collected on each patient are periodically analyzed, and the findings are reported and discussed with all centres participating in the national network. Regional health authorities are responsible for the accreditation of the reference centres in regional hospitals, which are linked to the Child and Adolescent NeuroPsychiatric Services (CANPS) located in the local communities. Thus, the reference centres are the specialized hubs of the CANPS network on ADHD and there is a close association between the reference centre and the CANPS. The reference centre is responsible for confirming the diagnosis and verifying the appropriateness of the therapeutic plan established by the CANPS. The reference centre also ensures the interface between the family paediatrician and the Mental Health Services (MHS) and guarantees the monthly visit and renewal of the drug prescription, as well as the behaviour therapy carried out by the CANPS. The Italian ADHD Registry therefore represents a distinctive tool; a unique experience in the international context that assures the appropriate care and safety of drug use in ADHD children.

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Competing interests: None declared

Author's reply to Timimi

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5 November 2013

Given the increasing costs of stimulant use¹ and the convincing argument that there is insufficient evidence “that the benefits outweigh the harms” in long term use for ADHD “of any severity”,² isn't it now time for the Health Department to investigate the cost-benefit profile for such drug use? In order to decide what is the best approach for our children, we need to balance the playing field. Government should match the considerable financial investment that has gone into investigation of drug treatments for ADHD (funded directly or indirectly by pharmaceutical companies) and commission research into the side effect consequences of current methylphenidate use by affected children.

We need a serious investigation into alternative educational options for children with ADHD. Why should they always have to sit and listen? What if ADHD is an evolutionary strategy which has contemporary value? It has taken two million years to evolve human beings, but just two hundred to develop modern education. If children with ADHD are a square peg in the round hole of mainstream provision, why can't we change the shape of the hole? Isn't that a safer and cheaper alternative to iatrogenic growth retardation and spiraling drug budgets?

I agree with Timimi that we must strive to diminish subjectivity bias in assessment of psychiatric conditions. Currently, ADHD assessment is weak in this respect. I disagree with Timimi in my belief that the use of a semi-structured interview³ for patients presenting with possible autism (even in pre-school children) has successfully increased assessment objectification, not just of behavioural differences, but also of thinking differences presented by patients⁴. If ADHD research cannot deliver an equally valid and reliable form of direct clinical assessment, questions about whether ADHD is a psychiatric condition of childhood (i.e. a difference of thinking, as well as of behaviour, which the patient can report and the clinician can elicit) are bound to increase.

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Competing interests: I am an Autism Diagnostic Observation Schedule (ADOS) trainer and have been paid for co-leading a training course; I have been paid by the Scottish government to co-lead research into autism assessment in Scotland; I am chair of the review of the SIGN guideline on autism spectrum disorders.

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